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A. 発明の属する分野の分類（国際特許分類（IPC））

Int.Cl⁶ C07C311/00, C07D209/20, C07D403/12, C07D207/16, C07D233/56, C07D213/52, C07D213/40, C07D295/13, A61K31/405, A61K31/415, A61K31/40, A61K31/195, A61K31/18, A61K31/215, A61K31/44, A61K31/535

B. 調査を行った分野

調査を行った最小限資料（国際特許分類（IPC））

Int.Cl⁶ C07C311/00, C07D209/20, C07D403/12, C07D207/16, C07D233/56, C07D213/52, C07D213/40, C07D295/13, A61K31/405, A61K31/415, A61K31/40, A61K31/195, A61K31/18, A61K31/215, A61K31/44, A61K31/535

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース（データベースの名称、調査に使用した用語）

CAS ONLINE

C. 関連すると認められる文献

引用文献のカテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する請求の範囲の番号
x	JP, 62-181296, A (コミツサリア タ レネルギー アトミーク) 8.8月.1987 (08.08.87)&EP, 203865, A2&US, 4736019, A&CA, 1288046, C	1, 2, 4
x	K. KAMAHORI et al., "Synthesis of Polymer-Supported Chiral N-Sulfonylamino Acids and Their Use in Asymmetric Diels-Alder Reaction of Cyclopentadiene with Methacrolein", Tetrahedron :Asymmetry, (1995) Vol. 6, No. 10, P. 2547-2555	1, 2, 4
x	V. BERTINI et al., "Synthesis of functionalized benzenesulfonyl monomers, polymers and copolymers designed for the selective flocculation of aqueous smithonite dispersions", Eur. Polym. J. (1992), Vol. 28, No. 10, P. 1225-1229	1, 2, 4

☒ C欄の続きにも文献が列挙されている。

☐ パテントファミリーに関する別紙を参照。

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「P」国際出願日前で、かつ優先権の主張の基礎となる出願の日の後に公表された文献
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「&」同一パテントファミリー文献

国際調査を完了した日	国際調査報告の発送日
22.07.97	05.08.97

国際調査機関の名称及びあて先
日本国特許庁（ISA/JP）
郵便番号100
東京都千代田区霞が関三丁目4番3号

特許庁審査官（権限のある職員）
渡辺 陽子 印 4H 9279

電話番号 03-3581-1101 内線 3443

C（続き）．　関連すると認められる文献

引用文献のカテゴリー＊	引用文献名　及び一部の箇所が関連するときは、その関連する箇所の表示	関連する請求の範囲の番号
x	E. DULOS et al., "Adsorption of plasma proteins onto anticoagulant polystyrene derivatives:a fluorescence study", Biomaterials, (1988)Vol. 9, No. 5, P. 405-412	1, 2, 4
x	N. DEBAILLOU et al., "Adsorption of human albumin and fibrinogen onto heparin-like materials", Colloids and Surfaces, (1985)Vol. 16, No. 3-4, P. 271-288	1, 2, 4
A	JP, 6-256293, A (チバ　ガイギー　アクチエン　ゲゼルシヤフト) 13.9月.1994(13.09.94)&CA, 2112779, A&US, 5455258, A&US, 5552419, A&US, 5506242, A&EP, 606046, A2	1-16

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DIALOG(R)File 351:DERWENT WPI

011133084 **Image available**
WPI Acc No: 97-111008/**199711**
XRAM Acc No: C97-035485
Use of new or known benzene-sulphonyl aminoacid derivs. - for treating diseases mediated by metalloprotease activity
Patent Assignee: ONO PHARM CO LTD (ONOY)
Inventor: KANAZAWA H; MIYAZAKI T; OHNO H; SAKAKI K; SUGIURA T
Number of Countries: 018 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 757037	A2	19970205	EP 96305554	A	19960729	C07C-311/42	199711 B
JP 9309875	A	19971202	JP 96213272	A	19960725	C07C-311/19	199807

Priority Applications (No Type Date): JP 9690491 A 19960319; JP 95212556 A 19950728
Cited Patents: No-SR.Pub
Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
EP 757037	A2	E	146			
JP 9309875	A		96			

Designated States (Regional): AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE

Abstract (Basic): EP 757037 A

Use of benzenesulphonamide derivs. of formula (I) or their salts is claimed for the prepn. of medicaments for preventing and/or treating diseases induced by overexpression or excess activity of metalloproteases. R1 = H or alkyl; R2 = H, 1-8C alkyl, phenyl, or alkyl (substd. by phenyl, OCOR16 or CONR17R18; R16 = 1-4C alkyl; R17, R18 = H or 1-4C alkyl; E = CONR3, NR3CO, CO-O, O-CO, NR3CONR3, CO-CH2, CO, OCONR3, NR3CO-O, O-CO-O, CS-NR3, NR3-CS, NR3-CS-NR3, O-CS-NR3, NR3-CS-O, CS-O, O-CS or O-CS-O; R3 = H, alkyl, phenyl or phenylalkyl; A = H, 1-8C alkyl, 3-7C cycloalkyl or Ar; Ar = aryl or heteroaryl (both opt. substd. by 1-3 of 1-15C alkyl, 1-15C alkoxy, halo, NO2, CN, guanidino, amidino, OH, benzyloxy, NH2, mono- or di-alkylamino, COOR'', CF3, Ph or heterocyclyl; J = a bond, 2-4C alkylene, 2-4C alkenylene or CR4R5; R4, R5 = H, alkyl or alkoxy; or CR4R5 = 3-7C cycloalkyl; G = (CH2)m or CR6R7; m = 2-4; R6, R7 = H, 1-8 C alkyl (opt. substd. by COOR8, alkoxy, OH, benzyloxy, NR12R13, NR14COOR15, Ar or heterocyclyl, and when substd., a C atom in 1-8C alkyl may be replaced by S), COOR8, Ar or heterocyclyl; or CR6R7 = 3-7C cycloalkyl; R8, R15 = H, 1-8C alkyl, Ph or phenylalkyl; R11-R14 = H or alkyl; alkyl, alkoxy have 1-4C unless specified otherwise; provided that A is not H when J = a bond and E = O-CO-NR3, O-CO-O, O-CS-NR3 or O-CS-O.

Also claimed are cpds. (I) and their salts as defined above, with 71cpds. excluded, e.g. N-[[2,3 or 4-(benzoylamino)phenyl)sulphonyl)glycine.

USE - (I) are used for treating rheumatoid arthritis, arthrosteitis, abnormal bone resorption, osteoporosis, periodontitis, interstitial nephritis, arteriosclerosis, pulmonary emphysema, cirrhosis, corneal injury, metastasis, invasion or growth of tumour cells, autoimmune diseases, diseases caused by vascular leukocyte emigration or infiltration, or arterialisation (claimed), including Crohn's disease and Sjogren's syndrome; in animals esp. humans.

Dosage is 1-1000 mg orally, up to several times per day; or 1-100 mg parenterally.

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Title Terms: NEW; BENZENE; SULPHONYL; AMINOACID; DERIVATIVE; TREAT; DISEASE ; MEDIATOR; ACTIVE
Index Terms/Additional Words: METALLO; PROTEASE
Derwent Class: B05

International Patent Class (Main): C07C-311/19; C07C-311/42
International Patent Class (Additional): A61K-031/195; A61K-031/215; A61K-031/265; A61K-031/27; A61K-031/34; A61K-031/38; A61K-031/405; A61K-031/415; A61K-031/44; A61K-031/63; C07C-311/29; C07C-311/46; C07C-311/47; C07D-209/20; C07D-213/55; C07D-213/59; C07D-213/81; C07D-213/82; C07D-233/26; C07D-233/64; C07D-307/68; C07D-333/24; C07D-333/38; C07D-333/40
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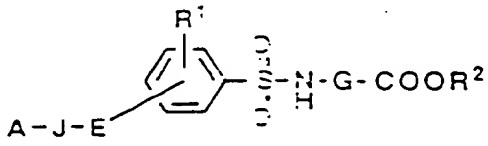
(54) Sulfonylamino acid derivatives as metalloproteinase inhibitors

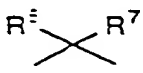
(57) The present invention relates to:

(i) matrix metalloproteinase (MMP) inhibitors containing sulfonylamino acid derivatives of the formula (Ia):



(Ia)

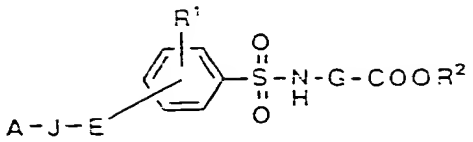
wherein R^1 is hydrogen, C1-4 alkyl; R^2 is hydrogen, C1-8 alkyl etc.; E is $-CONR^3-$, in which R^3 is hydrogen, C1-4 alkyl etc., $-NR^3CO-$, $-CO-O-$, $-O-CO-$ etc.; A is hydrogen, C1-8 alkyl, C3-7 cycloalkyl, or Ar; J is bond, C2-4 alkylene etc., G is $-(CH_2)_m-$, in which m is 2, 3 or 4, or



in which R^6 and R^7 is hydrogen, C1-6 alkyl etc., and non-toxic salts thereof,

(ii) novel sulfonylamino acid derivatives of the formula (Ib):

EP 0 757 037 A2



(Ib)

wherein all the symbols are as defined for formula (Ia). with the exclusion of certain compounds: and non-toxic salts thereof. and

(iii) processes for the preparation of the compounds of formula (Ib).

The compounds of formulae (Ia) and (Ib) are useful for prevention and/or treatment of diseases induced by over-expression or excess activity of MMP. such as rheumatoid diseases. arthrosteitis, unusual bone resorption. osteoporosis. periodontitis. interstitial nephritis. arteriosclerosis. pulmonary emphysema. cirrhosis. cornea injury, metastasis. invasion or growth of tumor cells. autoimmune diseases (Crohn's disease, Sjogren's syndrome etc.), diseases caused by vascular emigration or infiltration of leukocytes. or arterialization.

Description

This invention relates to sulfonylamino acid derivatives and matrix metalloproteinase inhibitors containing sulfonylamino acid derivatives as active ingredient. More particularly, this invention relates to:

(i) matrix metalloproteinase inhibitors containing sulfonylamino acid derivatives of the formula (Ia) as hereinafter defined, and non-toxic salts thereof, as active ingredient.
(ii) novel sulfonylamino acid derivatives of the formula (Ib) as hereinafter defined, and non-toxic salts thereof, and
(iii) processes for the preparation of the compounds of formula (Ib).

The matrix metalloproteinases (MMPs) are neutral metalloproteinases and zinc (Zn^{2+}) is essential in the active site for their activation. They degrade collagen, laminin, proteoglycans, fibronectin, elastin, gelatin etc. under physiological conditions and, therefore, are effective on growth and tissue remodeling of articulation tissue, bone tissue and connective tissue. At least 10 classes of MMPs which differ in primary structure are identified.

As common characteristics of these enzymes, MMPs

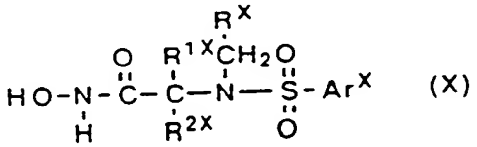
(1) have Zn^{2+} in the active site and the activity depends on calcium (Ca^{2+}),
(2) are secreted as an inactive proenzyme and activated outside of cells,
(3) have high homology on amino acid sequence,
(4) have an ability to degrade various extracellular matrix components in vivo,
(5) are regulated by tissue inhibitors of metalloproteinases (TIMP) which are specific to MMPs.

MMP inhibitors are useful for prevention and / or treatment of various diseases induced by overexpression or excess activation of MMP. Such diseases are, for example, rheumatoid diseases, arthrosteitis, unusual bone resorption, osteoporosis, periodontitis, interstitial nephritis, arteriosclerosis, pulmonary emphysema, cirrhosis, cornea injury, metastasis of, invasion of or growth of tumor cells, autoimmune diseases (e.g. Crohn's disease, Sjogren's syndrome), diseases caused by vascular emigration or infiltration of leukocytes, arterialization.

Some compounds possessing inhibitory activity against MMP are known. A sequence in the vicinity of the cleavage site of collagen (Gly-Ile-Ala-Gly or Gly-Leu-Ala-Gly) has high affinity for collagenase.

Much research and development on substrate analogous MMP inhibitors, which are chemically modified so as to have zinc affinity groups on a cleavage site of the substrate, has energetically been carried out [Inhibitors of matrix metalloproteinases (MMPs). Nigel RA Beeley, Phillip RJ Ansell, Andrew JP Docherty et al., Curr. Opin. Ther. Patents, 4, 7-16 (1994). Current Drugs Ltd ISSN 0962-2594]. However, these substrate-analogous inhibitors might have various problems. Therefore, it is desired to obtain a non-peptide inhibitor and some compounds are reported.

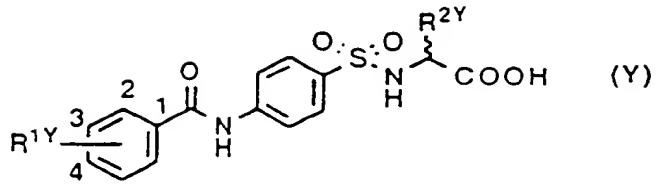
For example, in the specification of EP 606046, aryl-sulfonamide derivatives of the formula (X):



(X)

wherein (a) Ar^x is carbocyclic or heterocyclic aryl; R^x is hydrogen, lower alkyl, carbocyclic aryl-lower alkyl etc.; R^{1x} is hydrogen, lower alkyl, carbocyclic aryl-lower alkyl etc.;
R^{2x} is hydrogen, lower alkyl; or (b) R^x and R^{1x} together with the chain to which they are attached form 1,2,3,4-tetrahydro-isoquinoline, piperidine etc.; Ar^x and R^{2x} are as defined in (a); or (c) R^{1x} and R^{2x} together with the carbon to which they are attached form C3-7 cycloalkane, oxa-cyclohexane, thia-cyclohexane etc. which is unsubstituted or substituted by lower alkyl; and Ar^x and R^{2x} are as defined in (a);
inter alia, are disclosed to have inhibitory activity against matrix metalloproteinase.

Phenylsulfonylamino acid derivatives of the formula (Y):



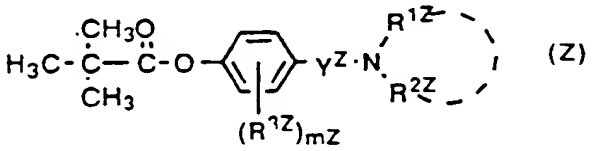
(Y)

wherein

R^{1y} is hydrogen, R^{2y} is hydrogen;
R^{1y} is 4-methoxy, R^{2y} is hydrogen;
R^{1y} is 4-fluoro, R^{2y} is hydrogen;
R^{1y} is 4-nitro, R^{2y} is hydrogen;
R^{1y} is 3-nitro, R^{2y} is hydrogen;
R^{1y} is 2-nitro, R^{2y} is hydrogen;
R^{1y} is 4-formyl, R^{2y} is hydrogen;
R^{1y} is hydrogen, R^{2y} is (S)-phenyl;
R^{1y} is hydrogen, R^{2y} is (R)-phenyl;
R^{1y} is 4-methyl, R^{2y} is (S)-phenyl;
R^{1y} is 4-methyl, R^{2y} is (R)-phenyl;
R^{1y} is 4-methoxy, R^{2y} is (S)-phenyl;
R^{1y} is 4-methoxy, R^{2y} is (R)-phenyl;
R^{1y} is 4-fluoro, R^{2y} is (S)-phenyl;
R^{1y} is 4-fluoro, R^{2y} is (R)-phenyl;
R^{1y} is 4-nitro, R^{2y} is (S)-phenyl; or
R^{1y} is 4-nitro, R^{2y} is (R)-phenyl;

inter alia, are disclosed to have inhibitory activity against aldose reductase [Biochemical Pharmacology, 40, 2219-2226 (1990)].

In the specification of EP347168, p-substituted phenyl esters of pivalic acid derivatives of the formula (Z):



(Z)

wherein Y^z is sulfonyl (-SO_2-) or carbonyl (-CO-); R^{1z} and R^{2z}, same or different, is hydrogen, C1-16 alkyl which may be substituted by carboxy (-COOH); R^{3z} is hydrogen, hydroxy, C1-6 alkyl, halogen, C1-4 alkoxy or C2-5 acyloxy; m^z is 1-4; inter-alia, are disclosed to have inhibitory activity against elastase.

The following compounds, inter alia, are disclosed to possess antimicrobial activity [J. Serb. Chem. Soc. 56(6), 311-316 (1991)].

N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-alanine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-β-alanine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-valine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-leucine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-serine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-phenylalanine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-alanine methyl ester,

N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine methyl ester.
N-[[4-(2 4-Dichlorobenzoylamino)phenyl]sulfonyl]-D.L-valine methyl ester.
N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine methyl ester.
N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-D.L-serine methyl ester. and
N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine methyl ester.

The following compounds, inter alia. are disclosed to possess antifilarial activity [Indian J. Chem. 30B. 182-187 (1991)]

N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid.
N-[[3-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
N-[[4-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid and
N- [[3-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid.

The following compounds. inter alia. are disclosed to possess antineoplastic activity [Indian J. Chem. 28B. 843-847 (1989)].

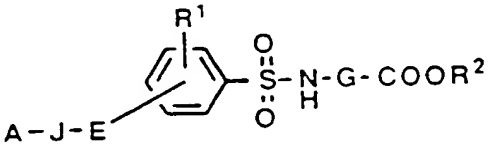
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-glutamic acid.
N-[[4-(4-chlorobenzoylamino)phenyl]sulfonyl]-L-glutamic acid and
N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-glutamic acid.

Energetic investigations have been carried out in order to make a matrix metalloproteinase inhibitor. The present inventors have found that a series of sulfonylamino acid derivatives of the formula (Ia) have inhibitory activity against matrix metalloproteinase and have accomplished the present invention.

Sulfonylamino acid derivatives of the formula (Ia) of the present invention are not known as matrix metalloproteinase inhibitors at all. And sulfonylamino acid derivatives of the formula (Ib) of the present invention are novel compounds that are not known at all.

Moreover. the compounds of the present invention possess. especially, a selective inhibitory activity against gelatinases classified in matrix metalloproteinases.

The present invention provides the use of a compound of formula (Ia):



(Ia)

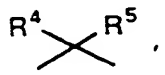
wherein

R^1 is hydrogen, or C1-4 alkyl;
R^2 is (1) hydrogen, (2) C1-8 alkyl, (3) phenyl. or (4) C1-4 alkyl substituted by phenyl, $-OCOR^{16}$, in which R^{16} is C1-4 alkyl: or $-CONR^{17}R^{18}$, in which R^{17} and R^{18} each, independently, is hydrogen or C1-4 alkyl;
E is

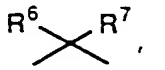
(1) $-CONR^3-$, in which R^3 is hydrogen, C1-4 alkyl, phenyl, or C1-4 alkyl substituted by phenyl;
(2) $-NR^3CO-$, in which R^3 is as hereinbefore defined:
(3) -CO-O-.
(4) -O-CO-.
(5) $-NR^3-CO-NR^3-$, in which R^3 is as hereinbefore defined:
(6) $-CO-CH_2-$,
(7) -CO-.
(8) $-O-CO-NR^3-$, in which R^3 is as hereinbefore defined:
(9) $-NR^3-CO-O-$, in which R^3 is as hereinbefore defined:
(10) -O-CO-O-,
(11) $-CS-NR^3-$, in which R^3 is as hereinbefore defined:
(12) $-NR^3-CS-$, in which R^3 is as hereinbefore defined:

(13) -NR^3-CS-NR^3-, in which R^3 is as hereinbefore defined;
(14) -O-CS-NR^3-, in which R^3 is as hereinbefore defined;
(15) -NR^3-CS-O-, in which R^3 is as hereinbefore defined;
(16) -CS-O-,
(17) -O-CS-, or
(18) -O-CS-O-.

A is (1) hydrogen, (2) C1-8 alkyl, (3) C3-7 cycloalkyl, or (4) Ar, in which Ar is carbocyclic aryl or heterocyclic aryl, and is unsubstituted or substituted by 1-3 of C1-15 alkyl, C1-15 alkoxy, halogen, nitro, cyano, guanidino, amidino, hydroxy, benzyloxy, -NR^9R^{10}, in which R^9 and R^{10} each, independently, is hydrogen or C1-4 alkyl; -$COOR^{11}$, in which R^{11} is hydrogen or C1-4 alkyl; trifluoromethyl, phenyl or heterocyclic ring;
J is (1) a bond, (2) C2-4 alkylene, (3) C2-4 alkenylene, or (4)

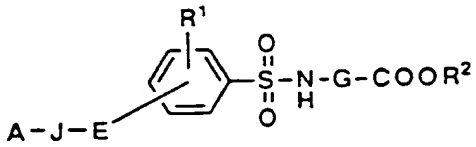


in which R^4 and R^5 each, independently, is (i) hydrogen, (ii) C1-4 alkyl, or (iii) C1-4 alkoxy, or R^4 and R^5, taken together with the carbon to which they are attached, form a C3-7 cycloalkyl group.
G is (1) - $(CH_2)_m$-, in which m is 2, 3 or 4, or (2)



in which R^6 and R^7 each, independently, is (i) hydrogen, (ii) C1-8 alkyl, (iii) -$COOR^8$, in which R^8 is hydrogen, C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl; (iv) Ar, in which Ar is as hereinbefore defined; (v) heterocyclic ring, (vi) C1-8 alkyl substituted by: -$COOR^8$, in which R^8 is as hereinbefore defined; C1-4 alkoxy; hydroxy; benzyloxy; -$NR^{12}R^{13}$, in which R^{12} and R^{13} each, independently, is hydrogen or C1-4 alkyl; -$NR^{14}COOR^{15}$, in which R^{14} is hydrogen or C1-4 alkyl, and R^{15} is hydrogen, C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl; Ar; or heterocyclic ring; with the proviso that one of the carbon atoms in C1-8 alkyl may be replaced by a sulfur atom; or R^6 and R^7, taken together with the carbon to which they are attached, form a C3-7 cycloalkyl group;
with the proviso that, when E is -O-CO-NR^3-, -O-CO-O-, -O-CS-NR^3- or -O-CS-O-, and J is a bond, A is not hydrogen;
or a non-toxic salt thereof, in the manufacture of a medicament for the prevention and/or treatment of a disease induced by overexpression or excess activity of a metalloproteinase.

The present invention also provides a compound of formula (Ib):



(Ib)

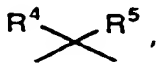
wherein

R^1 is hydrogen, or C1-4 alkyl;
R^2 is (1) hydrogen, (2) C1-8 alkyl, (3) phenyl, or (4) C1-4 alkyl substituted by phenyl, -$OCOR^{16}$, in which R^{16} is C1-4 alkyl; or -$CONR^{17}R^{18}$, in which R^{17} and R^{18} each, independently, is hydrogen or C1-4 alkyl;
E is

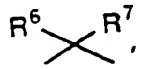
(1) -$CONR^3$-, in which R^3 is hydrogen, C1-4 alkyl, phenyl, or C1-4 alkyl substituted by phenyl;
(2) -NR^3CO-, in which R^3 is as hereinbefore defined;
(3) -CO-O-.

(4) -O-CO-
(5) -NR^3-CO-NR^3- in which R^3 is as hereinbefore defined:
(6) -CO-CH_2-.
(7) -CO-.
(8) -O-CO-NR^3-. in which R^3 is as hereinbefore defined:
(9) -NR^3-CO-O-. in which R^3 is as hereinbefore defined:
(10) -O-CO-O-,
(11) -CS-NR^3-. in which R^3 is as hereinbefore defined:
(12) -NR^3-CS-. in which R^3 is as hereinbefore defined:
(13) -NR^3-CS-NR^3-. in which R^3 is as hereinbefore defined:
(14) -O-CS-NR^3-. in which R^3 is as hereinbefore defined:
(15) -NR^3-CS-O-. in which R^3 is as hereinbefore defined:
(16) -CS-O-.
(17) -O-CS-. or
(18) -O-CS-O-.

A is (1) hydrogen, (2) C1-8 alkyl, (3) C3-7 cycloalkyl, or (4) Ar. in which Ar is carbocyclic aryl or heterocyclic aryl, and is unsubstituted or substituted by 1-3 of C1-15 alkyl. C1-15 alkoxy, halogen. nitro. cyano, guanidino. amidino. hydroxy. benzyloxy, -NR^9R^{10}. in which R^9 and R^{10} each. independently, is hydrogen or C1-4 alkyl; -$COOR^{11}$, in which R^{11} is hydrogen or C1-4 alkyl; trifluoromethyl, phenyl or heterocyclic ring;
J is (1) a bond. (2) C2-4 alkylene. (3) C2-4 alkenylene. or (4)



in which R^4 and R^5 each, independently, is (i) hydrogen, (ii) C1-4 alkyl, or (iii) C1-4 alkoxy, or R^4 and R^5, taken together with the carbon to which they are attached. form a C3-7 cycloalkyl group,
G is (1) -$(CH_2)_m$-. in which m is 2. 3 or 4. or (2)



in which R^6 and R^7 each. independently, is (i) hydrogen, (ii) C1-8 alkyl, (iii) -$COOR^8$, in which R^8 is hydrogen, C1-8 alkyl. phenyl. or C1-4 alkyl substituted by phenyl: (iv) Ar, in which Ar is as hereinbefore defined: (v) heterocyclic ring. (vi) C1-8 alkyl substituted by: -$COOR^8$, in which R^8 is as hereinbefore defined; C1-4 alkoxy; hydroxy; benzyloxy: -$NR^{12}R^{13}$. in which R^{12} and R^{13} each, independently, is hydrogen or C1-4 alkyl: -$NR^{14}COOR^{15}$, in which R^{14} is hydrogen or C1-4 alkyl. and R^{15} is hydrogen. C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl; Ar; or heterocyclic ring: with the proviso that one of the carbon atoms in C1-8 alkyl may be replaced by a sulfur atom; or R^6 and R^7. taken together with the carbon to which they are attached. form a C3-7 cycloalkyl group;
with the proviso that, when E is -O-CO-NR^3-,-O-CO-O-,-O-CS-NR^3- or -O-CS-O-, and J is a bond, A is not hydrogen:
or a non-toxic salt thereof:
with the exclusion of the following compounds:

(54) N-[[4-[2-(4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester.
(55) N-[[4-[2-(4-(1-Nitrophenyl)butyryloxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
(56)N-[[4-(2-Methoxy-2-phenylacetyloxy)phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
(57) N-[[4-[[[1-(4-Nitrophenyl)cyclobutyl]carbonyl]-oxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
(58) N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-t-butoxycarbonyl-L-lysine,
(59) N- [[4- (2-Phenylbutyryloxy)phenyl]sulfonyl]glycine,
(60) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-phenylalanine,
(61) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-aspartic acid,
(62) N-[[4-[[[1-(4-Nitrophenyl)cyclobutyl]carbonyl]oxy]phenyl]sulfonyl]-D,L-aspartic acid,
(63) 1-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonylamide]-1-cyclopropanecarboxylic acid,
(64) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-furanyl)glycine,
(65) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-thienyl)glycine,

(66) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-valine.
(67) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-S-carboxymethyl-L-cysteine.
(68) N-[[4-[2-Ethyl-2-(4-methoxyphenyl)butyryloxy]phenyl]sulfonyl]-glycine.
(69) N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-lysine. and
(70) 5-[N-[[3-Methyl-4-[2-[4-(1-pyrrolidinyl)phenyl] butyryloxy]phenyl]sulfonyl]amino]pentanoic acid:

and with the exclusion of compounds specifically named and characterised in the prior art.

The following compounds are believed to be known:

(1) N- [[4-(Benzoylamino)phenyl]sulfonyl]glycine.
(2) N-[[3-(Benzoylamino)phenyl]sulfonyl]glycine.
(3) N- [[2-(Benzoylamino)phenyl]sulfonyl]glycine,
(4) N-[[4-(Acetylamino)phenyl]sulfonyl]glycine.
(5) N- [[4-(Phenylacetylamino)phenyl]sulfonyl]glycine.
(6) N-[[4-[(Phenylethylcarbonyl)amino]phenyl]sulfonyl]glycine,
(7) N-[[4-(Cinnamoylamino)phenyl]sulfonyl]glycine.
(8) N-[[4-(N-Phenylureido)phenyl]sulfonyl]glycine.
(9) N-[[4-(N-Phenylthioureido)amino]phenyl]sulfonyl]glycine.
(10) N-[[4-[(Benzyloxycarbonyl)amino]phenyl]sulfonyl]glycine,
(11) N-[[4-[(Phenyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine,
(12) N-[[4-[(Benzyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine.
(13) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]glycine.
(14) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]glycine.
(15) N- [[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]glycine.
(16) N- [[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(17) N-[[4-(2-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(18) N-[[4-(4-Formylbenzoylamino)phenyl]sulfonyl]glycine.
(19) N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(20) N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-α-phenylglycine.
(21) N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(22) N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(23) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-D-α-phenyl-glycine.
(24) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-L-α-phenyl-glycine,
(25) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-D-α-phenyl-glycine,
(26) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-L-α-phenyl-glycine,
(27) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-D-α-phenyl-glycine,
(28) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-α-phenyl-glycine,
(29) N-[(4-Pivaloyloxyphenyl)sulfonyl]-D,L-α-phenyl-glycine,
(30) N-[(4-Pivaloyloxyphenyl)sulfonyl]-D,L-phenylalanine,
(31) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-glycine.
(32) N- [[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl] -D. L-alanine,
(33) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-β-alanine,
(34) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine,
(35) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-valine,
(36) N-[[4-(2,4-Dichlorobenzoylaminolphenyl]sulfonyl]-L-leucine,
(37) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-leucine,
(38) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-serine,
(39) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-phenylalanine,
(40) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine.
(41) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-alanine methyl ester,
(42) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine methyl ester,
(43) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-valine methyl ester,
(44) N-[[4-[[(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine methyl ester,
(45) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-serine methyl ester,
(46) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine methyl ester,
(47) N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid.
(48) N-[[3-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
(49) N- [[4-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,

(50) N-[[3-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid.
(51) N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-glutamic acid.
(52) N-[[4-(4-chlorobenzoylamino)phenyl]sulfonyl]-L-glutamic acid.
(53) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-glutamic acid. and
(71) N-[[(3-Methyl-4-pivaloyloxy)phenyl]sulfonyl]-β-alanine.

The present invention also provides a process for the preparation of a compound of formula (Ib) or a non-toxic salt thereof.

Unless otherwise specified, all isomers are included in the present invention. For example, alkyl, alkoxy and alkylene include straight and branched isomers. Isomers resulting from the presence of asymmetric carbon(s) e.g. branched alkyl are also included within the present invention.

In the formulae (Ia) and (Ib), C1-4 alkyl represented by R^1, R^3, R^4, R^5, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{16}, R^{17}, or R^{18} means methyl, ethyl, propyl, butyl and isomeric groups thereof.

In the formulae (Ia) and (Ib), C1-8 alkyl represented by R^2, R^6, R^7, R^8, R^{15}, or A means methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl and isomeric groups thereof.

In the formulae (Ia) and (Ib), C1-4 alkyl substituted by phenyl represented by R^2, R^3, R^8, or R^{15} means methyl, ethyl, propyl, butyl and isomeric groups thereof substituted by 1 of phenyl.

In the formulae (Ia) and (Ib), C1-4 alkoxy represented by R^4, R^5, R^6, or R^7 means methoxy, ethoxy, propoxy, butoxy and isomeric groups thereof.

In the formulae (Ia) and (Ib), C1-15 alkyl as a substituent of Ar means methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl and isomeric groups thereof.

In the formulae (Ia) and (Ib), C1-15 alkoxy as a substituent of Ar means methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy, heptyloxy, octyloxy, nonyloxy, decyloxy, undecyloxy, dodecyloxy, tridecyloxy, tetradecyloxy, pentadecyloxy and isomeric groups thereof.

In the formulae (Ia) and (Ib), halogen as a substituent of Ar is fluorine, chlorine, bromine or iodine.

In the formulae (Ia) and (Ib), C2-4 alkylene represented by J means ethylene, trimethylene, tetramethylene and isomeric groups thereof.

In the formulae (Ia) and (Ib), C2-4 alkenylene represented by J means vinylene, propenylene, butenylene, butadienylene and isomeric groups thereof.

In the formulae (Ia) and (Ib), C3-7 cycloalkyl represented by R^4 and R^5, taken together with carbon to which they are attached, or by R^6 and R^7, taken together with carbon to which they are attached or by A means cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

In the formulae (Ia) and (Ib), carbocyclic aryl represented by A, or by Ar in R^6 or R^7 preferably means C5-10 carbocyclic aryl, for example, benzene, pentalene, indene, naphthalene, azulene.

In the formulae (Ia) and (Ib), heterocyclic aryl represented by A, or by Ar in R^6 and R^7 preferably means C5-15 membered mono- or bi-heterocyclic aryl containing 1-2 of nitrogen, 1 of oxygen and/or 1 of sulfur, for example, a radical derived from pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, azepine, diazepine, furan, pyran, oxepin, oxazepine, thiophene, thiain (thiopyran), thiepin, oxazole, isoxazole, thiazole, isothiazole, oxadiazole, oxazine, oxadiazine, oxazepine, oxadiazepine, thiadiazole, thiazine, thiadiazine, thiazepine, thiadiazepine, indole, isoindole, benzof-uran, isobenzofuran, benzothiophene, isobenzothiophene, indazole, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, benzoxazole, benzothiazole or benzoimidazole.

In the formulae (Ia) and (Ib), heterocyclic ring represented by R^6 or R^7, or present as a substitutent of Ar, preferably means C5-15 membered mono- or bi-heterocyclic ring containing 1-2 of nitrogen and/or 1 of oxygen and/or 1 of sulfur. The heterocyclic ring includes partially or fully saturated analogues of the above C5-15 membered mono- or bi-heterocyclic aryl containing 1-2 of nitrogen and/or 1 of oxygen and/or 1 of sulfur, for example, a radical derived from pyrroline, pyrrolidine, imidazoline, imidazolidine, pyrazoline, pyrazolidine, piperidine, piperazine, tetrahydropyrimidine, tetrahydropyridazine, dihydrofuran, tetrahydrofuran, dihydropyran, tetrahydropyran, dihydrothiophene, tetrahydrothiophene, dihydrothiain (dihydrothiopyran), tetrahydrothiain (tetrahydrothiopyran), dihydrooxazole, tetrahydrooxazole, dihydroisoxazole, tetrahydroisoxazole, dihydrothiazole, tetrahydrothiazole, dihydroisothiazole, tetrahydroisothiazole, morpholine, thiomorpholine, indoline, isoindoline, dihydrobenzofuran, perhydrobenzofuran, dihydroisobenzofuran, perhydrobenzofuran, dihydrobenzothiophene, perhydrobenzothiophene, dihydroisobenzothiophene, perhydroisobenzothiophene, dihydroindazole, perhydroindazole, dihydroquinoline, tetrahydroquinoline, perhydroquinoline, dihydroisoquinoline, tetrahydroisoquinoline, perhydroisoquinoline, dihydrophthalazine, tetrahydrophthalazine, perhydrophthalazine, dihydronaphthyridine, tetrahydronaphthyridine, perhydronaphthyridine, dihydroquinoxaline, tetrahydroquinoxaline, perhydroquinoxaline, dihydroquinazoline, tetrahydroquinazoline, perhydroquinazoline, dihydrocinnoline, tetrahydrocinnoline, perhydrocinnoline, dihydrobenzoxazole, perhydrobenzoxazole, dihydrobenzothiazole, perhydrobenzothiazole, dihydrobenzimidazole or perhydrobenzimidazole.

In the present specification, including the claims, it is to be understood that the group E, as written, bonds to

benzene ring at the right side and to J at the left side. For example, when E is written as -CO-NR^3- the group AJE-bonded to the benzene ring is AJ-CO-NR^3-.

Non-toxic salts of the present invention include all pharmaceutically acceptable salts, for example, general salts, acid addition salts, hydrate salts.

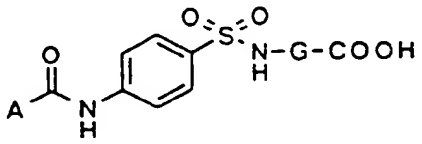
The compounds of formulae (Ia) and (Ib) of the present invention may be converted into the corresponding salts Water-soluble salts are preferred. Suitable salts, for example, include:
salts of alkali metals (e.g. sodium, potassium), salts of alkaline earth metals (e.g. calcium, magnesium), ammonium salts, salts of pharmaceutically acceptable organic amines (e.g. tetramethylammonium, triethylamine, methylamine, dimethylamine, cyclopentylamine, benzylamine, phenethylamine, piperidine, monoethanolamine, diethanolamine, tris (hydroxymethyl)amine, lysine, arginine, N-methyl-D-glucamine).

The compounds of formulae (Ia) and (Ib) may be converted into the corresponding acid addition salts. Water-soluble salts are preferred. Suitable salts, for example, include salts of inorganic acids e.g. hydrochloride, hydrobromide, hydroiodide, sulfate, phosphate, nitrate; salts of organic acids e.g. acetate, trifluoroacetate, lactate, tartarate, oxalate, fumarate, maleate, citrate, benzoate, methanesulphonate, ethanesulphonate, benzenesulphonate, toluenesulphonate, isethionate, glucuronate, gluconate.

The compounds of formulae (Ia) and (Ib) and salts thereof may be converted into the corresponding hydrates by conventional means.

In the compounds of the present invention of formulae (Ia) and (Ib), sulfonylamino acid derivatives of the following formulae, ester derivatives thereof and non-toxic salts thereof are preferred:

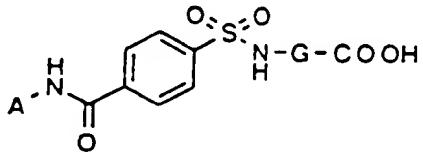
the formula I(1):



I (1)

wherein A and G are as hereinbefore defined,

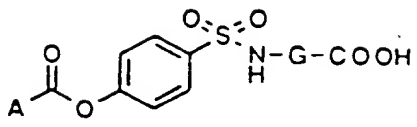
the formula I(2):



I (2)

wherein A and G are as hereinbefore defined.

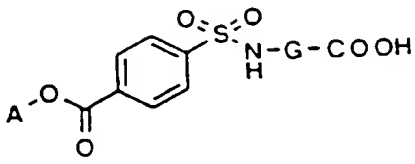
the formula I(3):



I (3)

wherein A and G are as hereinbefore defined.

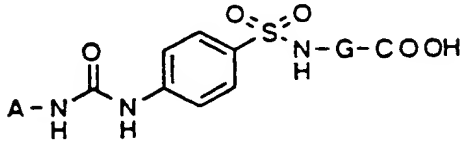
the formula I(4):



I (4)

wherein A and G are as hereinbefore defined.

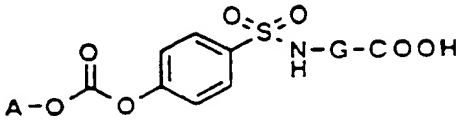
the formula I(5):



I (5)

wherein A and G are as hereinbefore defined.

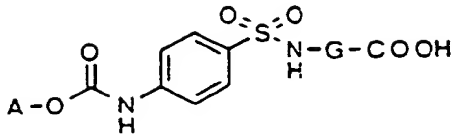
the formula I(6):



I (6)

wherein A and G are as hereinbefore defined.

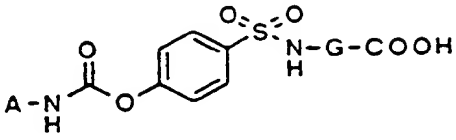
the formula I(7):



I (7)

wherein A and G are as hereinbefore defined.

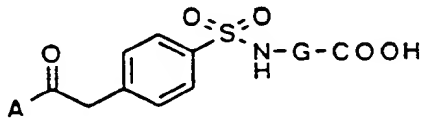
the formula I(8):



I (8)

wherein A and G are as hereinbefore defined.

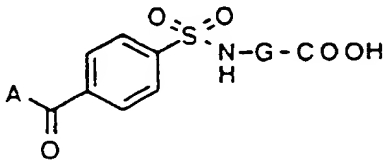
the formula I(9):



I (9)

wherein A and G are hereinbefore defined.

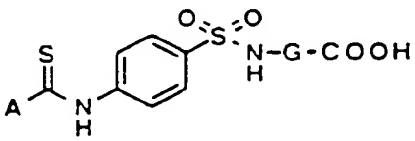
the formula I(10):



I (10)

wherein A and G are as hereinbefore defined.

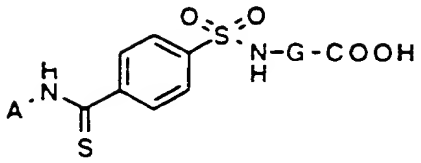
the formula I(11):



I (11)

wherein A and G are as hereinbefore defined.

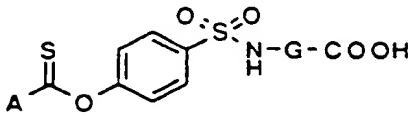
the formula I(12):



I (12)

wherein A and G are as hereinbefore defined.

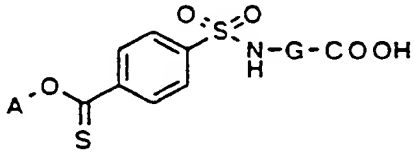
the formula I(13):



I (13)

wherein A and G are as hereinbefore defined.

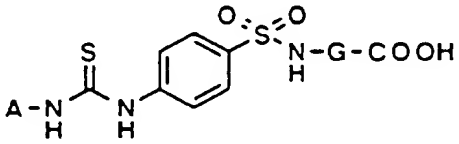
the formula I(14):



I (14)

wherein A and G are as hereinbefore defined.

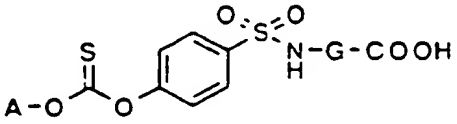
the formula I(15):



I (15)

wherein A and G are as hereinbefore defined.

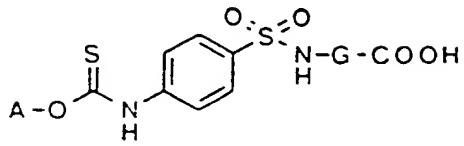
the formula I(16):



I (16)

wherein A and G are as hereinbefore defined.

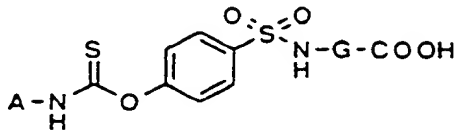
the formula I(17):



I (17)

wherein A and G are as hereinbefore defined.

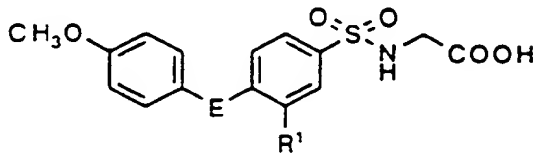
the formula I(18):



I (18)

wherein A and G are as hereinbefore defined.

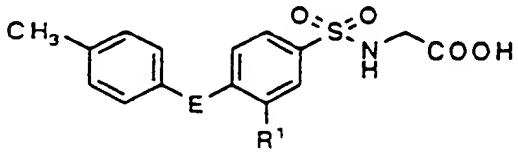
the formula I(19):



I (19)

wherein R^1 and E are as hereinbefore defined.

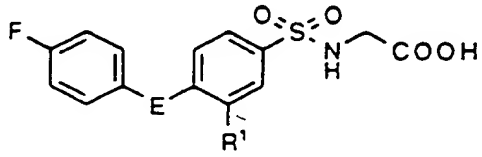
the formula I(20):



I (20)

wherein R^1 and E are as hereinbefore defined.

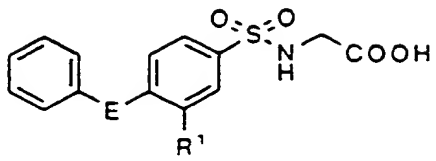
the formula I(21):



I (21)

wherein R^1 and E are as hereinbefore defined,

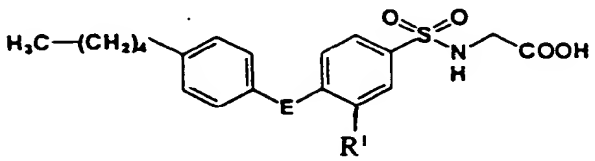
the formula I(22):



I (22)

wherein R^1 and E are as hereinbefore defined.

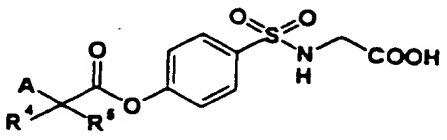
the formula I(23):



I (23)

wherein R^1 and E are as hereinbefore defined. and

the formula I(24):

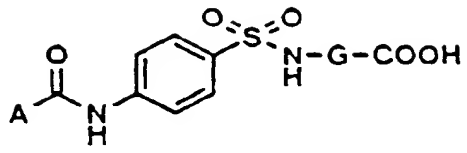


I (24)

wherein A, R^4 and R^5 are as hereinbefore defined.

The preferred specific compounds of formulae (Ia) and (Ib) are the compounds in Tables 1-23, the compounds numbered (1)-(71) following Table 23, the compounds described in the Examples, ester derivatives thereof and non-toxic salts thereof.

Table 1



(IA)

No.	A	G
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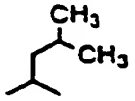
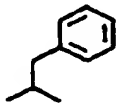
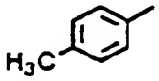
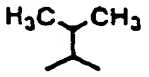
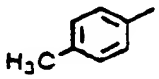
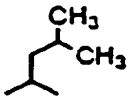
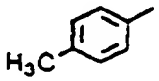
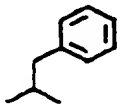
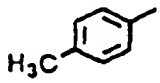
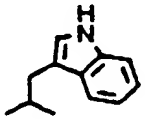
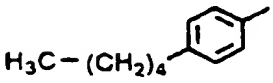
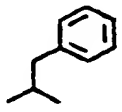
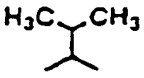
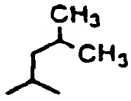
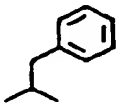
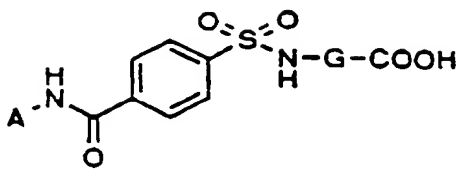
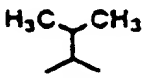
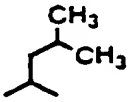
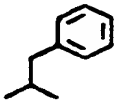
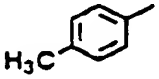
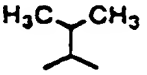
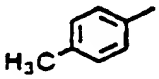
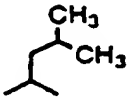
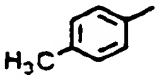
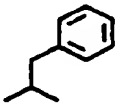
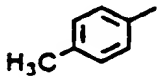
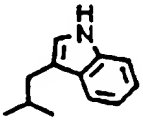
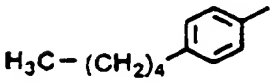
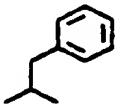
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

Table 2



(IB)

No.	A	G
1		
2		
3		
4		
5		
6		
7		
8		
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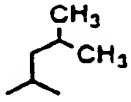
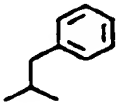
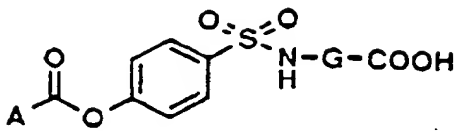
10		
11		

Table 3



(IC)

No.	A	G
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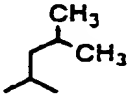
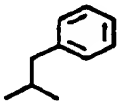
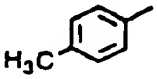
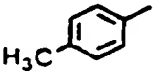
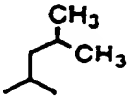
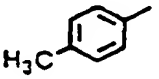
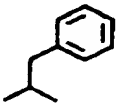
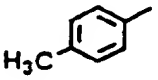
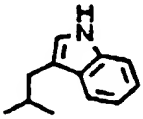
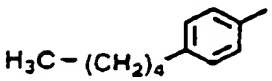
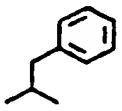
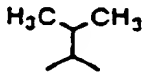
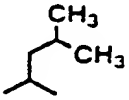
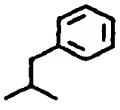
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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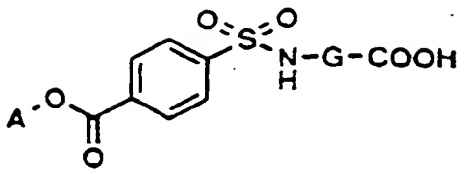

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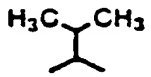
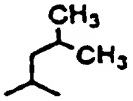
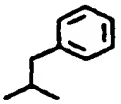
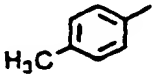
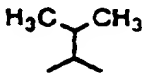
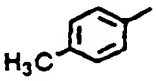
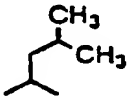
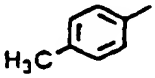
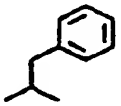
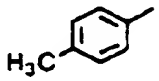
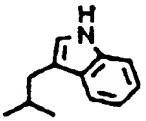
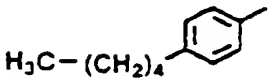
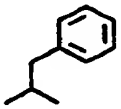
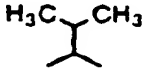
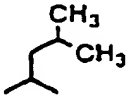
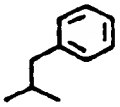
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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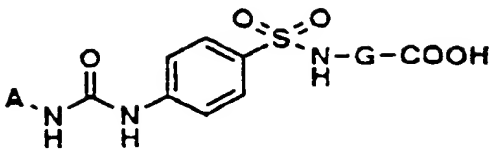

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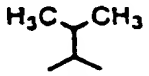
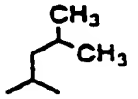
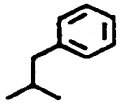
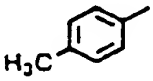
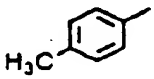
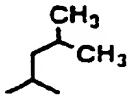
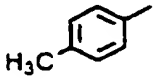
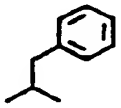
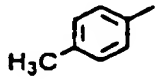
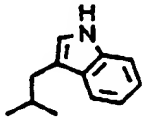
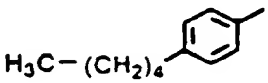
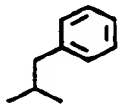
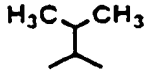
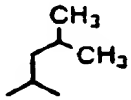
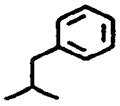
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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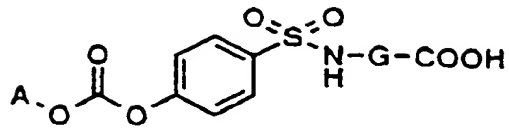

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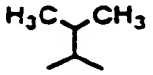
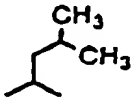
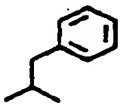
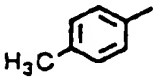
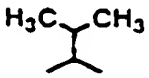
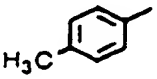
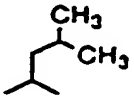
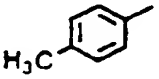
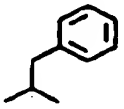
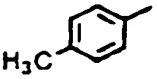
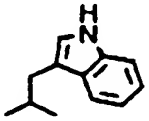
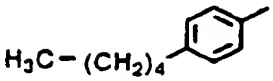
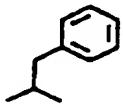
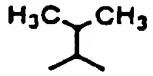
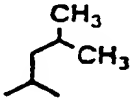
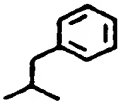
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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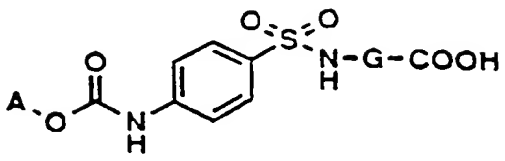

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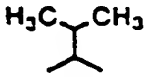
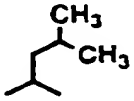
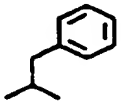
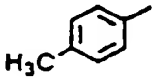
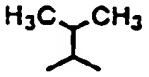
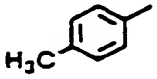
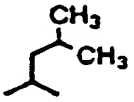
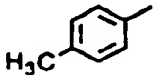
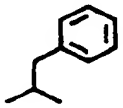
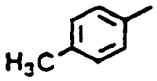
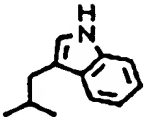
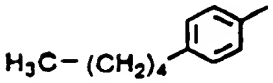
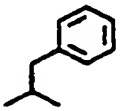
1		
2		
3		
4		
5		
6		
7		
8		
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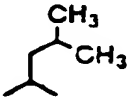
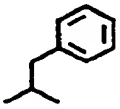
10		
11		

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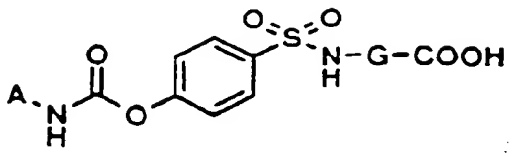

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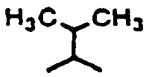
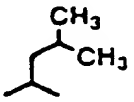
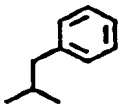
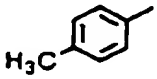
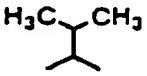
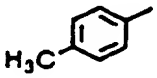
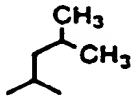
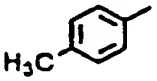
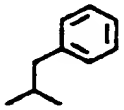
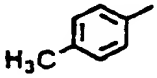
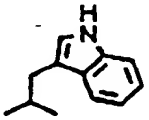
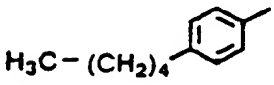
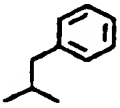
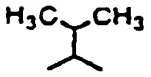
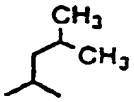
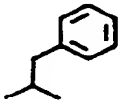
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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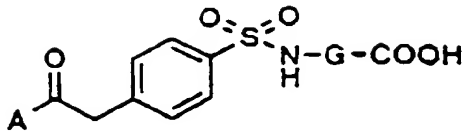

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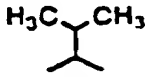
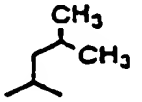
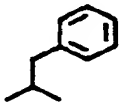
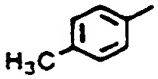
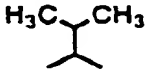
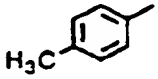
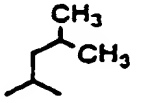
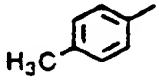
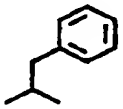
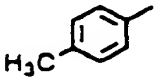
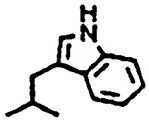
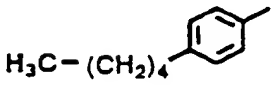
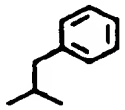
1		
2		
3		
4		
5		
6		
7		
8		
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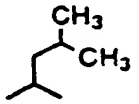
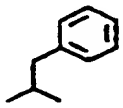
10		
11		

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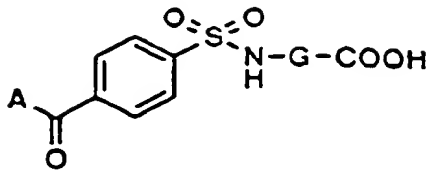

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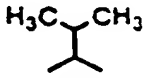
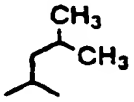
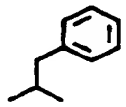
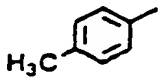
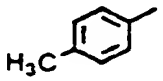
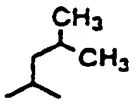
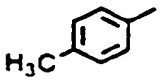
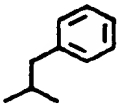
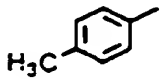
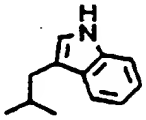
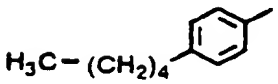
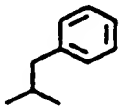
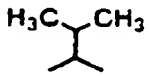
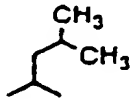
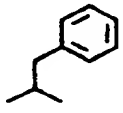
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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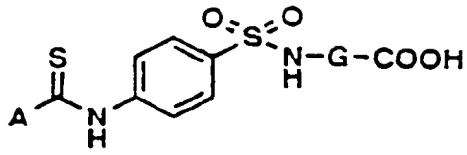

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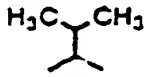
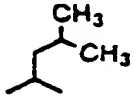
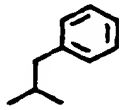
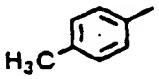
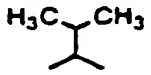
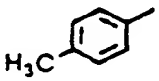
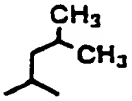
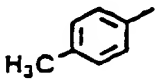
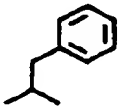
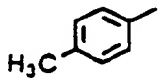
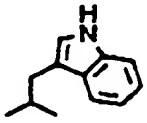
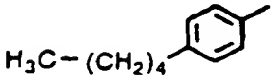
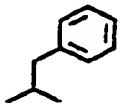
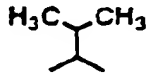
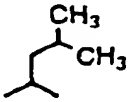
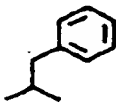
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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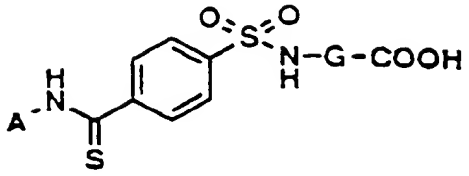

(IM)

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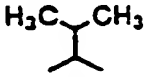
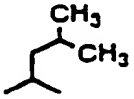
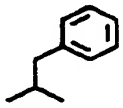
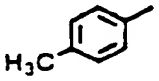
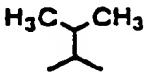
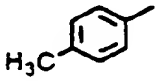
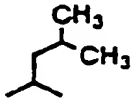
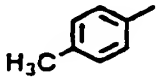
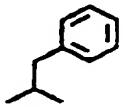
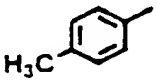
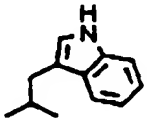
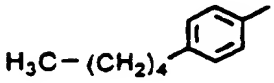
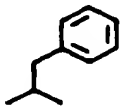
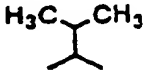
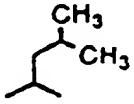
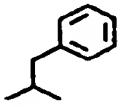
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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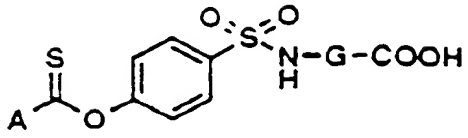

(IN)

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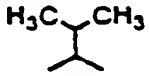
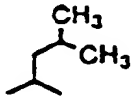
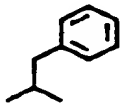
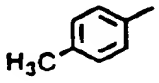
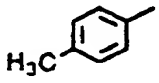
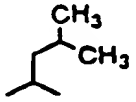
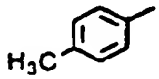
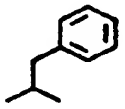
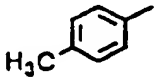
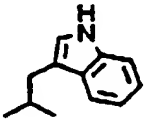
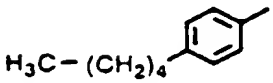
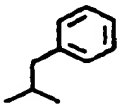
1		
2		
3		
4		
5		
6		
7		
8		
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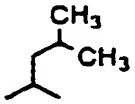
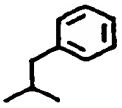
10		
11		

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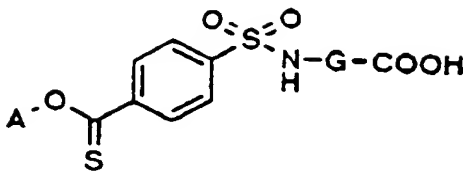

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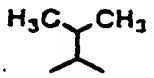
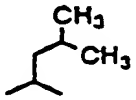
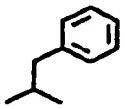
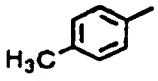
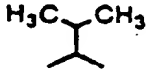
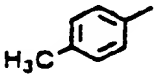
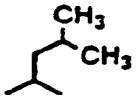
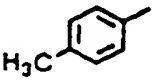
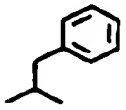
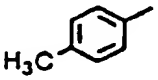
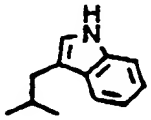
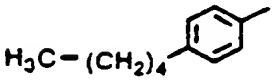
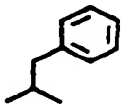
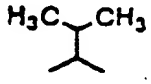
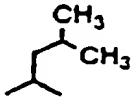
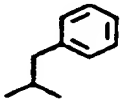
No.	A	G
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

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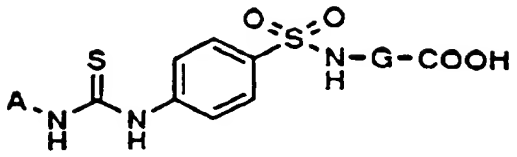

(IQ)

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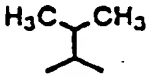
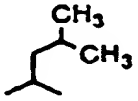
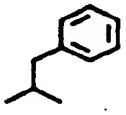
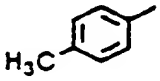
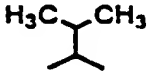
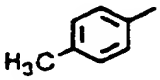
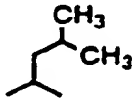
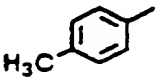
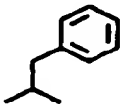
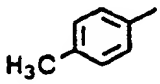
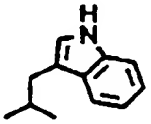
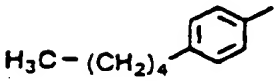
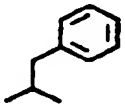
1		
2		
3		
4		
5		
6		
7		
8		
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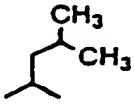
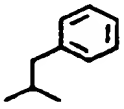
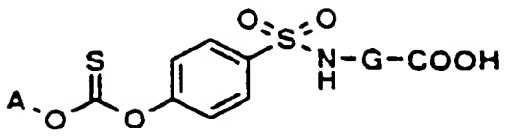
10		
11		

Table 16



(IR)

No.	A	G
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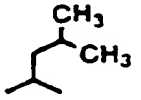
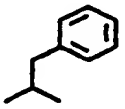
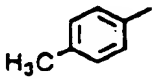
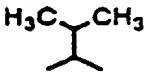
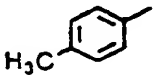
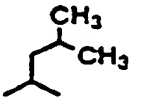
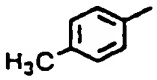
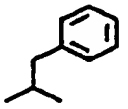
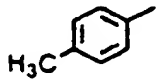
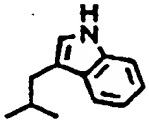
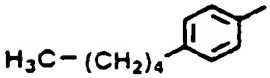
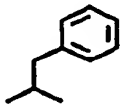
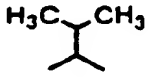
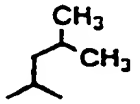
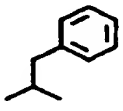
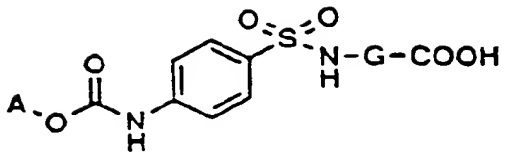
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

Table 17



(IS)

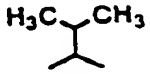
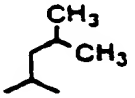
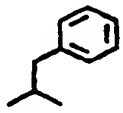
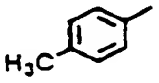
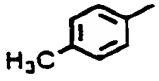
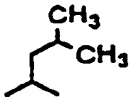
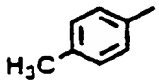
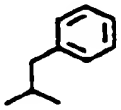
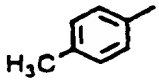
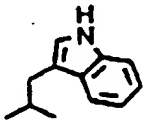
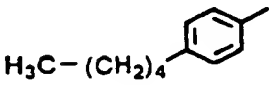
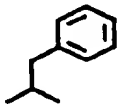
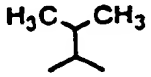
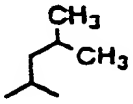
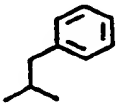
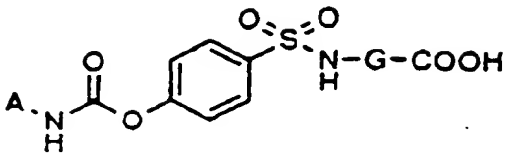
No.	A	G
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

Table 18



(IT)

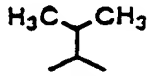
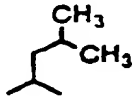
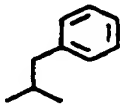
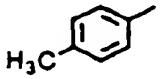
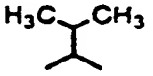
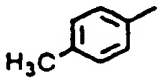
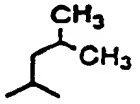
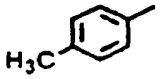
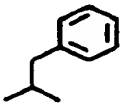
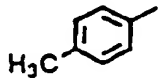
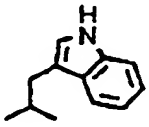
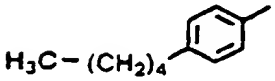
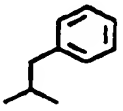
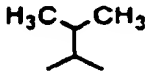
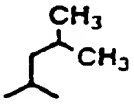
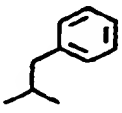
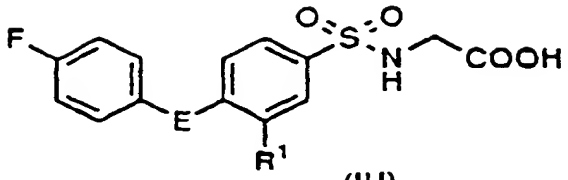
No.	A	G
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

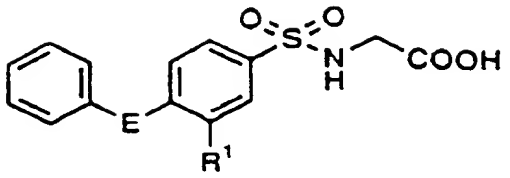
Table 19



(IU)

NO.	E	R^1
1	-CO-NH-	CH_3
2	-CO-NH-	$CH(CH_3)_2$
3	-NH-CO-	CH_3
4	-NH-CO-	$CH(CH_3)_2$
5	-CO-O-	CH_3
6	-CO-O-	$CH(CH_3)_2$
7	-O-CO-	CH_3
8	-O-CO-	$CH(CH_3)_2$
9	-NH-CO-NH-	CH_3
10	-NH-CO-NH-	$CH(CH_3)_2$
11	-O-CO-O-	CH_3
12	-O-CO-O-	$CH(CH_3)_2$
13	-O-CO-NH-	CH_3
14	-O-CO-NH-	$CH(CH_3)_2$
15	-NH-CO-O-	CH_3
16	-NH-CO-O-	$CH(CH_3)_2$
17	-CO-CH_2-	CH_3
18	-CO-CH_2-	$CH(CH_3)_2$
19	-CO-	CH_3
20	-CO-	$CH(CH_3)_2$
21	-CS-NH-	CH_3
22	-CS-NH-	$CH(CH_3)_2$
23	-NH-CS-	CH_3
24	-NH-CS-	$CH(CH_3)_2$
25	-CS-O-	CH_3
26	-CS-O-	$CH(CH_3)_2$
27	-O-CS-	CH_3
28	-O-CS-	$CH(CH_3)_2$
29	-NH-CS-NH-	CH_3
30	-NH-CS-NH-	$CH(CH_3)_2$
31	-O-CS-O-	CH_3
32	-O-CS-O-	$CH(CH_3)_2$
33	-O-CS-NH-	CH_3
34	-O-CS-NH-	$CH(CH_3)_2$
35	-NH-CS-O-	CH_3
36	-NH-CS-O-	$CH(CH_3)_2$

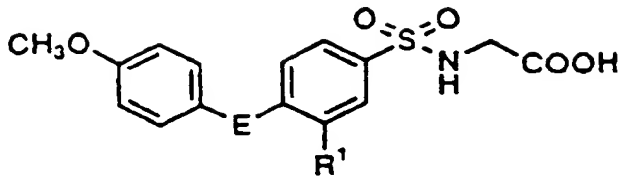
Table 20



(IW)

NO.	E	R^1
1	-CO-NH-	CH_3
2	-CO-NH-	$CH(CH_3)_2$
3	-NH-CO-	CH_3
4	-NH-CO-	$CH(CH_3)_2$
5	-CO-O-	CH_3
6	-CO-O-	$CH(CH_3)_2$
7	-O-CO-	CH_3
8	-O-CO-	$CH(CH_3)_2$
9	-NH-CO-NH-	CH_3
10	-NH-CO-NH-	$CH(CH_3)_2$
11	-O-CO-O-	CH_3
12	-O-CO-O-	$CH(CH_3)_2$
13	-O-CO-NH-	CH_3
14	-O-CO-NH-	$CH(CH_3)_2$
15	-NH-CO-O-	CH_3
16	-NH-CO-O-	$CH(CH_3)_2$
17	-CO-CH_2-	CH_3
18	-CO-CH_2-	$CH(CH_3)_2$
19	-CO-	CH_3
20	-CO-	$CH(CH_3)_2$
21	-CS-NH-	CH_3
22	-CS-NH-	$CH(CH_3)_2$
23	-NH-CS-	CH_3
24	-NH-CS-	$CH(CH_3)_2$
25	-CS-O-	CH_3
26	-CS-O-	$CH(CH_3)_2$
27	-O-CS-	CH_3
28	-O-CS-	$CH(CH_3)_2$
29	-NH-CS-NH-	CH_3
30	-NH-CS-NH-	$CH(CH_3)_2$
31	-O-CS-O-	CH_3
32	-O-CS-O-	$CH(CH_3)_2$
33	-O-CS-NH-	CH_3
34	-O-CS-NH-	$CH(CH_3)_2$
35	-NH-CS-O-	CH_3
36	-NH-CS-O-	$CH(CH_3)_2$

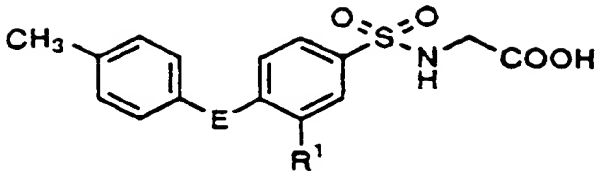
Table 21



(IY)

NO.	E	R^1
1	-CO-NH-	CH_3
2	-CO-NH-	$CH(CH_3)_2$
3	-NH-CO-	CH_3
4	-NH-CO-	$CH(CH_3)_2$
5	-CO-O-	CH_3
6	-CO-O-	$CH(CH_3)_2$
7	-O-CO-	CH_3
8	-O-CO-	$CH(CH_3)_2$
9	-NH-CO-NH-	CH_3
10	-NH-CO-NH-	$CH(CH_3)_2$
11	-O-CO-O-	CH_3
12	-O-CO-O-	$CH(CH_3)_2$
13	-O-CO-NH-	CH_3
14	-O-CO-NH-	$CH(CH_3)_2$
15	-NH-CO-O-	CH_3
16	-NH-CO-O-	$CH(CH_3)_2$
17	$-CO-CH_2-$	CH_3
18	$-CO-CH_2-$	$CH(CH_3)_2$
19	-CO-	CH_3
20	-CO-	$CH(CH_3)_2$
21	-CS-NH-	CH_3
22	-CS-NH-	$CH(CH_3)_2$
23	-NH-CS-	CH_3
24	-NH-CS-	$CH(CH_3)_2$
25	-CS-O-	CH_3
26	-CS-O-	$CH(CH_3)_2$
27	-O-CS-	CH_3
28	-O-CS-	$CH(CH_3)_2$
29	-NH-CS-NH-	CH_3
30	-NH-CS-NH-	$CH(CH_3)_2$
31	-O-CS-O-	CH_3
32	-O-CS-O-	$CH(CH_3)_2$
33	-O-CS-NH-	CH_3
34	-O-CS-NH-	$CH(CH_3)_2$
35	-NH-CS-O-	CH_3
36	-NH-CS-O-	$CH(CH_3)_2$

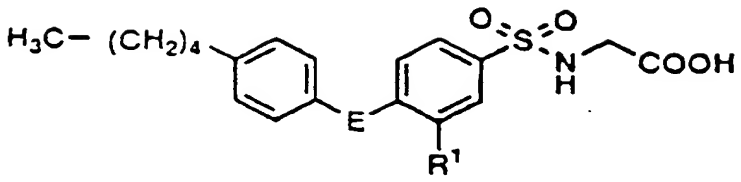
Table 22



(IZ)

NO.	E	R^1
1	-CO-NH-	CH_3
2	-CO-NH-	$CH(CH_3)_2$
3	-NH-CO-	CH_3
4	-NH-CO-	$CH(CH_3)_2$
5	-CO-O-	CH_3
6	-CO-O-	$CH(CH_3)_2$
7	-O-CO-	CH_3
8	-O-CO-	$CH(CH_3)_2$
9	-NH-CO-NH-	CH_3
10	-NH-CO-NH-	$CH(CH_3)_2$
11	-O-CO-O-	CH_3
12	-O-CO-O-	$CH(CH_3)_2$
13	-O-CO-NH-	CH_3
14	-O-CO-NH-	$CH(CH_3)_2$
15	-NH-CO-O-	CH_3
16	-NH-CO-O-	$CH(CH_3)_2$
17	-CO-CH_2-	CH_3
18	-CO-CH_2-	$CH(CH_3)_2$
19	-CO-	CH_3
20	-CO-	$CH(CH_3)_2$
21	-CS-NH-	CH_3
22	-CS-NH-	$CH(CH_3)_2$
23	-NH-CS-	CH_3
24	-NH-CS-	$CH(CH_3)_2$
25	-CS-O-	CH_3
26	-CS-O-	$CH(CH_3)_2$
27	-O-CS-	CH_3
28	-O-CS-	$CH(CH_3)_2$
29	-NH-CS-NH-	CH_3
30	-NH-CS-NH-	$CH(CH_3)_2$
31	-O-CS-O-	CH_3
32	-O-CS-O-	$CH(CH_3)_2$
33	-O-CS-NH-	CH_3
34	-O-CS-NH-	$CH(CH_3)_2$
35	-NH-CS-O-	CH_3
36	-NH-CS-O-	$CH(CH_3)_2$

Table 23



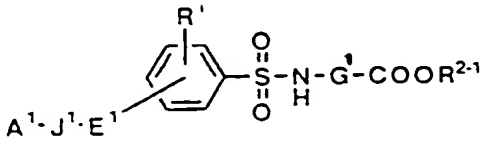
(IAA)

NO.	E	R^1
1	-CO-NH-	CH_3
2	-CO-NH-	$CH(CH_3)_2$
3	-NH-CO-	CH_3
4	-NH-CO-	$CH(CH_3)_2$
5	-CO-O-	CH_3
6	-CO-O-	$CH(CH_3)_2$
7	-O-CO-	CH_3
8	-O-CO-	$CH(CH_3)_2$
9	-NH-CO-NH-	CH_3
10	-NH-CO-NH-	$CH(CH_3)_2$
11	-O-CO-O-	CH_3
12	-O-CO-O-	$CH(CH_3)_2$
13	-O-CO-NH-	CH_3
14	-O-CO-NH-	$CH(CH_3)_2$
15	-NH-CO-O-	CH_3
16	-NH-CO-O-	$CH(CH_3)_2$
17	-CO-CH_2-	CH_3
18	-CO-CH_2-	$CH(CH_3)_2$
19	-CO-	CH_3
20	-CO-	$CH(CH_3)_2$
21	-CS-NH-	CH_3
22	-CS-NH-	$CH(CH_3)_2$
23	-NH-CS-	CH_3
24	-NH-CS-	$CH(CH_3)_2$
25	-CS-O-	CH_3
26	-CS-O-	$CH(CH_3)_2$
27	-O-CS-	CH_3
28	-O-CS-	$CH(CH_3)_2$
29	-NH-CS-NH-	CH_3
30	-NH-CS-NH-	$CH(CH_3)_2$
31	-O-CS-O-	CH_3
32	-O-CS-O-	$CH(CH_3)_2$
33	-O-CS-NH-	CH_3
34	-O-CS-NH-	$CH(CH_3)_2$
35	-NH-CS-O-	CH_3
36	-NH-CS-O-	$CH(CH_3)_2$

(1) N-[[4-(Benzoylamino)phenyl]sulfonyl]glycine.
(2) N-[[3-(Benzoylamino)phenyl]sulfonyl]glycine.
(3) N-[[2-(Benzoylamino)phenyl]sulfonyl]glycine.
(4) N-[[4-(Acetylamino)phenyl]sulfonyl]glycine.
(5) N-[[4-(Phenylacetylamino)phenyl]sulfonyl]glycine.
(6) N-[[4-[(Phenylethylcarbonyl)amino]phenyl]sulfonyl]glycine.
(7) N-[[4-(Cinnamoylamino)phenyl]sulfonyl]glycine,
(8) N-[[4-(N-Phenylureido)phenyl]sulfonyl]glycine.
(9) N-[[4-(N-Phenylthioureido)amino]phenyl]sulfonyl]glycine.
(10) N-[[4-[(Benzyloxycarbonyl)amino]phenyl]sulfonyl]glycine,
(11) N-[[4-[(Phenyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine,
(12) N-[[4-[(Benzyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine,
(13) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]glycine.
(14) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]glycine,
(15) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(16) N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(17) N-[[4-(2-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(18) N-[[4-(4-Formylbenzoylamino)phenyl]sulfonyl]glycine,
(19) N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(20) N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(21) N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(22) N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(23) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(24) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(25) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(26) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(27) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(28) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(29) N-[(4-Pivaloyloxyphenyl)sulfonyl]-D. L-α-phenylglycine,
(30) N-[(4-Pivaloyloxyphenyl)sulfonyl]-D. L-phenylalanine,
(31) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]glycine,
(32) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-alanine,
(33) N-[[4-(2, 4-Dichlorobenzoylamino)phenyl]sulfonyl]-β-alanine,
(34) N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine,
(35) N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-valine,
(36) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine,
(37) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-leucine,
(38) N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-serine.
(39) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-phenylalanine,
(40) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine,
(41) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-alanine methyl ester.
(42) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine methyl ester,
(43) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-valine methyl ester,
(44) N-[[4-[[(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine methyl ester,
(45) N-[[4-(2. 4-Dichlorobenzoylamino)phenyl]sulfonyl]-D. L-serine methyl ester.
(46) N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine methyl ester,
(47) N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
(48) N-[[3-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid.
(49) N-[[4-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid.
(50) N-[[3-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
(51) N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-glutamic acid.
(52) N-[[4-(4-Chlorobenzoylamino)phenyl]sulfonyl]-L-glutamic acid.
(53) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-glutamic acid.
(54) N-[[4-[2-(4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
(55) N-[[4-[2-(4-(1-Nitrophenyl)butyryloxy]phenyl]sulfonyl]-D,L-3-morpholino alanine ethyl ester,
(56) N-[[4-(2-Methoxy-2-phenylacetyloxy)phenyl]sulfonyl]-D,L-3-morpholino alanine ethyl ester,
(57) N-[[4-[[[1-(4-Nitrophenyl)cyclobutyl]carbonyl]oxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
(58) N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-t-butoxycarbonyl-L-lysine,

(59) N-[[4-(2-Phenylbutyryloxy)phenyl]sulfonyl]glycine.
(60) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-phenyl alanine.
(61) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-aspartic acid.
(62) N-[[4-[[[1-(4-Nitrophenyl)cyclobutyl]carbonyl]oxy]phenyl]sulfonyl]-D, L-aspartic acid,
(63) 1-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonylamide]-1-cyclopropanecarboxylic acid.
(64) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-furanyl)glycine.
(65) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-thienyl)glycine.
(66) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-valine.
(67) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-S-carboxymethyl-L-cysteine.
(68) N-[[4-[2-Ethyl-2-(4-methoxyphenyl)butyryloxy]phenyl]sulfonyl]-glycine,
(69) N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-lysine,
(70) 5-[N-[[3-Methyl-4-[2-[4-(1-pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]amino]pentanoic acid, and
(71) N-[[(3-Methyl-4-pivaloyloxy)phenyl]sulfonyl]-β-alanine.

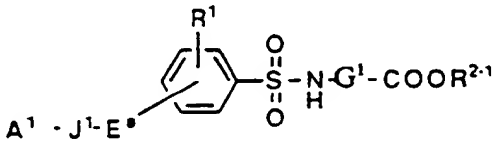
In the compounds of the present invention of the formula (Ib), the compound in which A-J-E-, substituents of Ar in A, R^6 and R^7 in G, and -$COOR^2$ are not -COOH or a group containing -COOH, and in which substituents of Ar in A, and R^6 and R^7 in G are not amino, hydroxy or a group containing amino or hydroxy, that is the compound of the formula (Ib-1):



(Ib-1)

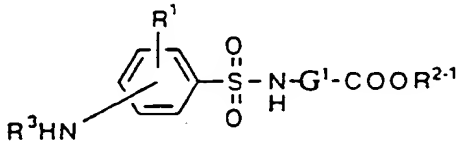
wherein R^{2-1} is C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl, -$OCOR^{16}$, in which R^{16} is as hereinbefore defined, or -$CONR^{17}R^{18}$, in which R^{17} and R^{18} are as hereinbefore defined; G^1, E^1, J^1 and A^1 are as hereinbefore defined for G, E, J and A, with the proviso that when E^1 is -OCO- or -OCS- and J^1 is a bond, A^1 is not hydrogen; and with the proviso that substituents of Ar in A^1, and R^6 and R^7 in G^1 are not -COOH, amino, hydroxy or a group containing -COOH, amino or hydroxy; and R^1 is as hereinbefore defined; may be prepared by following methods (a) - (k).

(a) In the compounds of the formula (Ib-1), the compounds in which E^1 is -$CONR^3$-, that is the compounds of the formula



(Ib-a)

wherein E^a is -CO-NR^3- and the other symbols are as hereinbefore defined;
may be prepared by amidation of the compound of the formula (IIb-a):



(IIb-a)

wherein all the symbols are as hereinbefore defined;
with the compound of the formula (IIIb-a):

A^1-J^1-COOH (IIIb-a)

wherein all the symbols are as hereinbefore defined: if necessary, followed by deprotection. (Ib-a):

The method of amidation is known. It includes the method

(1) via an acyl halide.
(2) via a mixed acid anhydride.
(3) using a condensing agent.

These methods are explained as follows.

(1) The method via an acyl halide, for example, may be carried out in an organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran) or without a solvent, using an acid halide (e.g. oxalyl chloride or thionyl chloride) at -20°C to reflux temperature, and the obtained acyl halide derivative may be reacted with an amine in an organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran) in the presence of a tertiary amine (e.g. pyridine, triethyl amine, dimethyl aniline or dimethylaminopyridine) at 0-40°C.
(2) The method via a mixed acid anhydride may be carried out, for example, by reacting a carboxylic acid with an acid halide (e.g. pivaloyl chloride, tosyl chloride, mesyl chloride, ethyl chloroformate or isobutyl chloroformate) in an organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran) or without a solvent, in the presence of a tertiary amine (e.g. pyridine, triethylamine, dimethylaniline or dimethylaminopyridine) at -20°C-40°C, and the obtained mixed acid anhydride derivative may be reacted with a corresponding amine in an organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran) at 0-40°C.
(3) The method using a condensing agent (e.g. 1,3-dicyclohexylcarbodiimide (DCC), 1-ethyl-3-[3-(dimethylamino) propyl]carbodiimide (EDC) or 2-chloro-1-methylpyridinium iodide) may be carried out, for example, by reacting a carboxylic acid with an amine in an organic solvent (e.g. chloroform, methylene chloride, dimethylformamide or diethyl ether) or without a solvent, optionally in the presence of a tertiary amine (e.g. pyridine, triethylamine, dimethylaniline or dimethylaminopyridine) using a condensing agent at 0-40°C.

The reactions described in (1), (2) and (3) may be carried out under an inert gas (e.g. argon or nitrogen) to avoid water in order to obtain a preferable result.

The method of deprotection is known. It includes

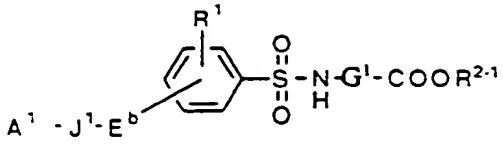
(1) deprotection under alkaline conditions,
(2) deprotection under acidic conditions,
(3) hydrogenolysis.

and a suitable method is selected from (1), (2) and (3) depending on the character of the protecting group.

These methods are explained as follows.

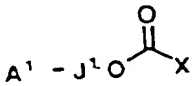
(1) Deprotection under alkaline conditions, for example, may be carried out in an organic solvent (e.g. methanol, tetrahydrofuran(THF) or dioxane), using an alkali metal hydroxide (e.g. potassium hydroxide or sodium hydroxide), an alkaline earth metal hydroxide (e.g. calcium hydroxide) or a carbonate (e.g. sodium carbonate or potassium carbonate), an aqueous solution thereof or a mixture thereof at 0-40°C.
(2) Deprotection under acidic conditions, for example, may be carried out in an organic solvent (e.g. methylene chloride, chloroform, dioxane, ethyl acetate, acetic acid, water or a mixture of two or more thereof), using an organic acid (e.g. trifluoroacetic acid), or an inorganic acid (e.g hydrogen chloride or hydrogen bromide) or a mixture thereof at 0-120°C.
(3) Hydrogenolysis, for example, may be carried out in a solvent [e.g. an ether (such as tetrahydrofuran, dioxane, dimethoxyethane or diethyl ether), an alcohol (such as methanol or ethanol), a benzene-type solvent (such as benzene or toluene), an amide (such as dimethylformamide), water, ethyl acetate, acetic acid or a mixture of two or more thereof], in the presence of a catalyst (e.g. palladium on carbon, palladium black, palladium hydroxide, platinum dioxide, or Raney-nickel), optionally in the presence of an inorganic acid (e.g. hydrochloric acid, sulfuric acid, hypochlorous acid, boric acid or tetrafluoroboric acid) or an organic acid (e.g. acetic acid, p-toluenesulfonic acid, oxalic acid, trifluoroacetic acid or formic acid), at ordinary or elevated pressure of hydrogen gas or ammonium formate at 0-200°C.

(b) In the compounds of the formula (Ib-1), the compounds in which E^1 is $-O-CO-NR^3-$, that is the compounds of the formula (Ib-b):



(Ib-b)

wherein E^b is $-O-CO-NR^3-$, and the other symbols are as hereinbefore defined;
may be prepared by reacting the above compound of the formula (IIb-a) with the compound of the formula (IIIb-b):



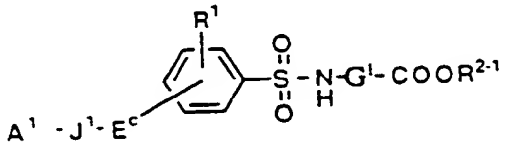
(IIIb-b)

wherein X is halogen and the other symbols are as hereinbefore defined;
if necessary, followed by deprotection.

This type of reaction is known and, for example, may be carried out in an organic solvent (e.g. acetonitrile or tetrahydrofuran) and optionally in the presence of water, using an organic base (e.g. 4-dimethylaminopyridine) or an inorganic base [e.g. an alkali metal hydroxide (such as sodium hydroxide or potassium hydroxide), an alkaline earth metal hydroxide (such as potassium hydroxide), or a carbonate (such as sodium carbonate or calcium carbonate)] at 0-40°C.

The reaction of deprotection may be carried out by the same method as hereinbefore described.

(c) In the compounds of the formula (Ib-1), the compounds in which E^1 is $-NR^3-CO-NR^3-$ or $-NR^3-CS-NR^3-$, that is the compounds of the formula (Ib-c):

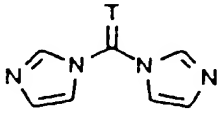


(Ib-c)

wherein E^c is $-NR^3-CO-NR^3-$ or $-NR^3-CS-NR^3-$, and the other symbols are as hereinbefore defined;
may be prepared by reacting the above compound of the formula (IIb-a) with the compound of the formula (IIIb-c):

(IIIb-c)

wherein all the symbols are as hereinbefore defined; and with the compound of the formula (IVb-c):



(IVb-c)

wherein T is oxygen or sulfur;
if necessary, followed by deprotection.

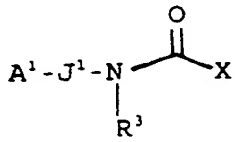
This type of reaction is known and, for example, may be carried out in an organic solvent (e.g. dimethylformamide, methylene chloride or tetrahydofuran), optionally in the presence of an amine (e.g. triethylamine, pyridine or dimethylaminopyridine) at 0-80°C.

The reaction of deprotection may be carried out by the same method as hereinbefore described.

Besides, it may be also prepared by reacting the above compound of the formula (IIb-a) with the compound of the formula (IIIb-c1):

$$A^1\text{-}J^1\text{-}N{=}C{=}O \qquad \text{(IIIb-c1)}$$

wherein all the symbols are as hereinbefore defined; or with the compound of the formula (IIIb-c2):



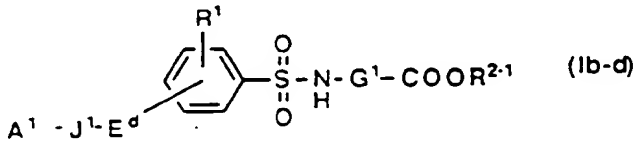
(IIIb-c2)

wherein all the symbols are as hereinbefore defined; if necessary, followed by deprotection.

This reaction is known and, for example, may be carried out in an organic solvent (e.g. acetone, chloroform, methyl chloride, benzene or tetrahydrofuran), optionally in the presence of an amine (e.g. triethylamine, pyridine or dimethylaminopyridine) at 0-80°C, or by the amidation method (1) via an acyl halide as hereinbefore described.

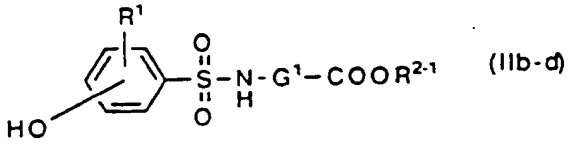
The reaction of deprotection may be carried out by the same method as hereinbefore described.

(d) In the compounds of the formula (Ib-1), the compounds in which E^1 is -CO-O-, that is the compounds of the formula (Ib-d):



(Ib-d)

wherein E^d is -CO-O- and the other symbols are as hereinbefore defined;
may be prepared by esterification of the compound of the formula (IIb-d):



(IIb-d)

wherein all the symbols are as hereinbefore defined; with the above compound of the formula (IIIb-a); if necessary, followed by deprotection.

The method of esterification is known. It includes the method

(1) via an acyl halide.
(2) using a mixed acid anhydride.
(3) using a condensing agent.

These methods are explained as follows.

(1) Acyl halide may be prepared in an organic solvent (e.g chloroform, methylene chloride, diethyl ether or tetrahydrofuran) or without a solvent, using an acid halide (e.g. oxalyl chloride or thionyl chloride) at -20°C to reflux temperature, and the obtained acyl halide derivative may be reacted with an alcohol derivative in an organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran), in the presence of a tertiary amine (e.g. pyridine, triethylamine, dimethylaniline or dimethylamino pyridine) at 0-40°C.

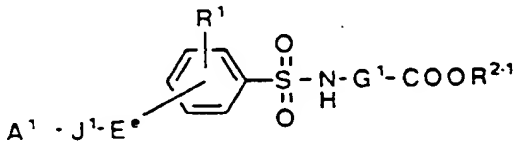
(2) Method using mixed acid anhydride may be carried out, for example, by reacting a carboxylic acid derivative with an acyl halide or acid derivative (e.g. ethyl chloroformate or isobutyl chloroformate), in an organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran) or without a solvent, in the presence of a tertiary amine (e.g pyridine, triethylamine, dimethylaniline or dimethylaminopyridine), and the obtained mixed acid anhydride derivative may be reacted with an alcohol derivative in an organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran) at 0-40°C.

(3) Method using a condensing agent (e.g. DCC, EDC or 2-chloro-1-methylpyridinium iodide) may be carried out, for example, by reacting a carboxylic acid derivative with an alcohol derivative in an organic solvent (e.g. chloroform, methylene chloride, dimethylformamide or diethyl ether) or without a solvent, in the optional presence of a tertiary amine (e.g. pyridine, triethylamine, dimethylaniline or dimethylaminopyridine), using a condensing agent at 0-40°C

The reactions described in (1), (2) and (3) may be carried out under an inert gas (e.g. argon or nitrogen) to avoid water in order to obtain a preferable result.

The reaction of deprotection may be carried out by the same method as hereinbefore described.

(e) In the compounds of the formula (Ib-1), the compounds in which E^1 is -O-CO-O-, that is the compounds of the formula (Ib-e):



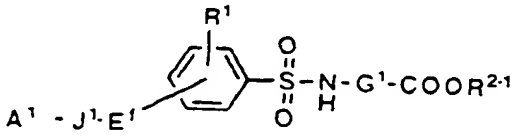
(Ib-e)

wherein E^e is -O-CO-O- and the other symbols are as hereinbefore defined;
may be prepared by reacting the above compound of the formula (IIb-d) with the above compound of the formula (IIIb-b), if necessary, followed by deprotection.

This reaction may be carried out by the same method as (b).

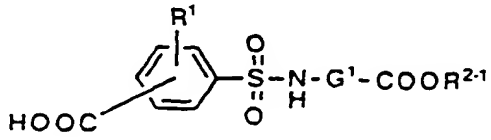
The reaction of deprotection may be carried out by the same method as hereinbefore described.

(f) In the compounds of the formula (Ib-1), the compounds in which E^1 is -NR^3-CO-, that is the compounds of the formula (Ib-f):



(Ib-f)

wherein E^f is -NR^3-CO- and the other symbols are as hereinbefore defined;
may be prepared by amidation of the compound of the formula (IIb-f):



(IIb-f)

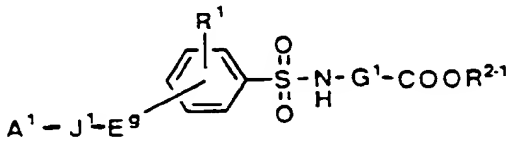
wherein all the symbols are as hereinbefore defined; with the above compound of the formula (IIIb-c) ; if necessary,

followed by deprotection

This reaction of amidation may be carried out by the same method as (a).

The reaction of deprotection may be carried out by the same method as hereinbefore described.

(g) In the compounds of the formula (Ib-1), the compounds in which E^1 is -O-CO-, that is the compounds of the formula (Ib-g):



(Ib-g)

wherein E^9 is -O-CO- and the other symbols are as hereinbefore defined;

may be prepared by esterification of the above compound of the formula (IIb-f) with the compound of the formula (IIIb-g):

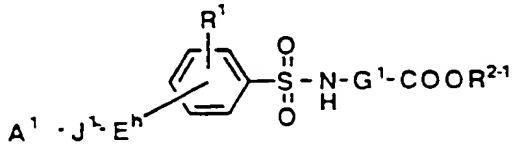
$$A^1\text{-}J^1\text{-}OH \qquad \text{(IIIb-g)}$$

wherein all the symbols are as hereinbefore defined: if necessary, followed by deprotection.

This reaction of esterification may be carried out by the same method as (d).

The reaction of deprotection may be carried out by the same method as hereinbefore described.

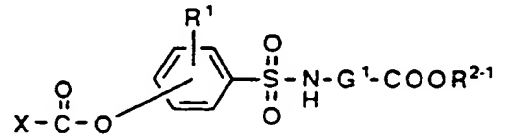
(h) In the compounds of the formula (Ib-1), the compounds in which E^1 is -NR^3-CO-O-, that is the compounds of the formula (Ib-h):



(Ib-h)

wherein E^h is -NR^3-CO-O- and the other symbols are as hereinbefore defined;

may be prepared by reacting the compound of the formula (IIb-h):



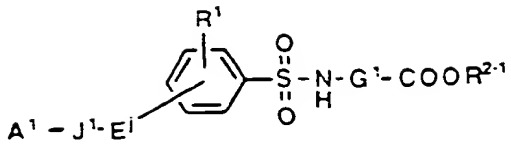
(IIb-h)

wherein all the symbols are as hereinbefore defined: with the above compound of the formula (IIIb-c): if necessary, followed by deprotection.

This reaction may be carried out by the same method as (b).

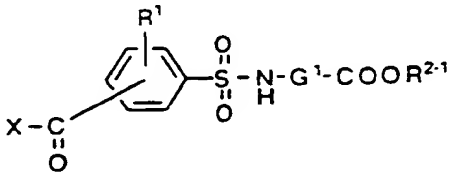
The reaction of deprotection may be carried out by the same method as hereinbefore described.

(j) In the compounds of the formula (Ib-1), the compounds in which E^1 is -CO- or -$CO\text{-}CH_2$- that is the compounds of the formula (Ib-j):



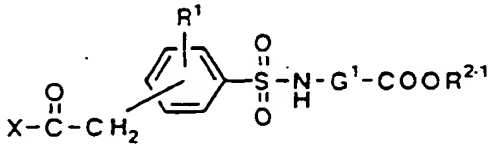
(Ib-j)

wherein E^1 is -CO- or -$CO-CH_2$- and the other symbols are as hereinbefore defined:
may be prepared by reacting the compound of the formula (IIb-j-1):



(IIb-j-1)

wherein all the symbols are as hereinbefore defined: or the compound of the formula (IIb-j-2):



(IIb-j-2)

wherein all the symbols are as hereinbefore defined; with the compound of the formula (IIIb-j):

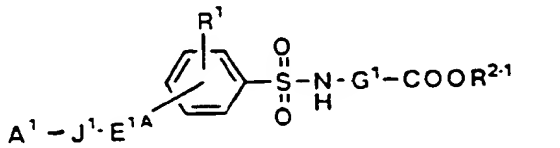
$$(A^1\text{-}J^1)_2CuLi \qquad \text{(IIIb-j)}$$

wherein all the symbols are as hereinbefore defined: if necessary, followed by deprotection.

This reaction using an organocopper agent is known: for example, an organocopper agent, which is prepared in organic solvent (e.g. tetrahydrofuran or ether), using an organic lithium agent and an inorganic copper compound (e. g. copper iodide or copper cyanide) at -78°C-0°C, may be reacted with an acyl halide at -78°C-0°C. The reactions may be carried out under an inert gas (e.g. argon or nitrogen) to avoid water in order to obtain a preferable result.

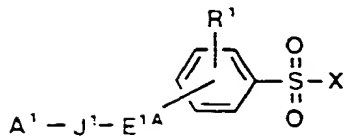
The reaction of deprotection may be carried out by the same method as hereinbefore described.

(j-1) In the compounds of the formula (Ib-1), the compounds in which E^1 is -$CO-NR^3$-, -$O-CO-NR^3$-, -NR^3-CO-O-, -CO-O-, -$CO-CH_2$- or -O-CO-O-, that is the compounds of the formula (Ib-1-AA):



(Ib-1-AA)

wherein E^{1A} is -$CO-NR^3$-, -$O-CO-NR^3$-, -NR^3-CO-O-, -CO-O-, -$CO-CH_2$- or -O-CO-O- and the other symbols are as hereinbefore defined:
may be prepared by amidation of the compound of the formula (XII):



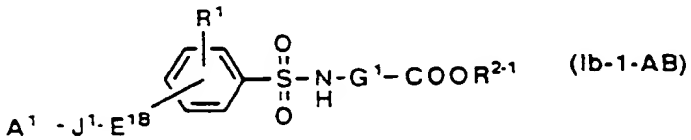
(XII)

wherein all the symbols are as hereinbefore defined:
with the compound of the formula (XIII):

$$H_2N\text{-}G^1\text{-}COOR^{2\text{-}1} \qquad \text{(XIII)}$$

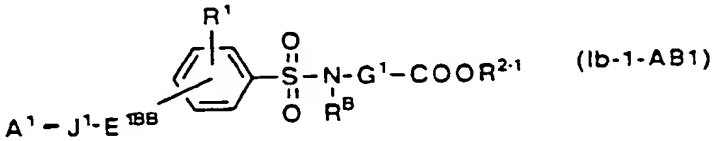
wherein all the symbols are as hereinbefore defined;
if necessary, followed by deprotection.

This amidation may be carried out by the amidation method (1) via an acyl halide as hereinbefore described.
The reaction of deprotection may be carried out by the same method as hereinbefore described.
(j-2) In the compounds of the formula (Ib-1), the compounds in which E^1 is -CO-NR^3-, -NR^3-CO-, -NR^3-CO-NR^3-, -O-CO-NR^3- or -NR^3-CO-O-, that is the compounds of the formula (Ib-1-AB):



(Ib-1-AB)

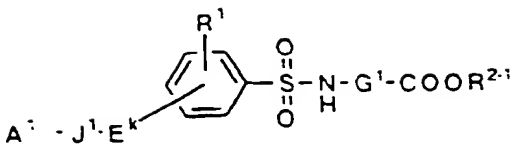
wherein E^{1B} is -CO-NR^3-, -NR^3-CO-, -NR^3-CO-NR^3-, -O-CO-NR^3- or -NR^3-CO-O- and the other symbols are as hereinbefore defined: may be also prepared by conversion of -NH- into -N($R^{3\text{-}1}$)-,
wherein $R^{3\text{-}1}$ is C1-4 alkyl, phenyl or C1-4 alkyl substituted by phenyl; in the compound of the formula (Ib-1-AB1):



(Ib-1-AB1)

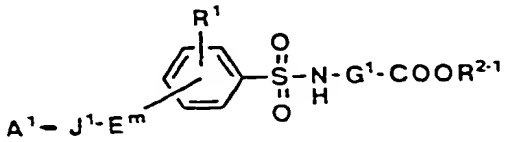
wherein E^{1BB} is -CO-NH-, -NH-CO-, -NH-CO-NH-, -O-CO-NH- or -NH-CO-O-, R^B is an amino-protecting group (e.g. t-butoxycarbonyl, benzyloxycarbonyl) and the other symbols are as hereinbefore defined;
and followed by deprotection of the amino group protected by R^B.

This reaction of conversion of -NH- into -N($R^{3\text{-}1}$)- may be performed in an organic solvent (e.g. dimethylformamide), in the presence of a base (e.g. sodium hydride), using a corresponding $R^{3\text{-}1}$-halide at 0-40°C.
The reaction of deprotection may be carried out by the same method as hereinbefore described.
(k) In the compounds of the formula (Ib-1), the compounds in which E^1 is -CS-NR^3-, -NR^3-CS-, -NR^3-CS-NR^3-, -O-CS-NR^3-, -NR^3-CS-O-, -CS-O-, -O-CS- or -O-CS-O- that is the compounds of the formula (Ib-k):



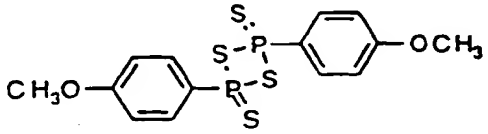
(Ib-k)

wherein E^k is -CS-NR^3-, -NR^3-CS-, -NR^3-CS-NR^3-, -O-CS-NR^3-, -NR^3-CS-O-, -CS-O-, -O-CS- or -O-CS-O- and the other symbols are as hereinbefore defined:
may be prepared by reacting the compound which is prepared by the above method, of the formula (IIb-a), (Ib-b), (Ib-c), (Ib-d), (Ib-e), (Ib-f), (Ib-g) or (Ib-h), that is the compound of the formula (Ib-m):



(Ib-m)

wherein E^m is -CO-NR^3-, -NR^3-CO-, -NR^3-CO-NR^3-, -O-CO-NR^3-, -NR^3-CO-O-, -CO-O-, -O-CO- or -O-CO-O- and the other symbols are as hereinbefore defined:
with Lawesson's reagent of the formula (IIIb-k):



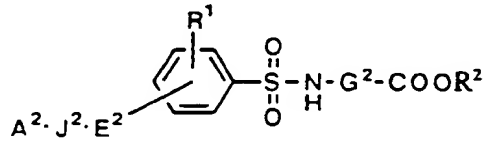
(IIIb-k)

if necessary, followed by deprotection.

This reaction using Lawesson's reagent is known and, for example, may be carried out in an organic solvent (e.g. dioxane, benzene, toluene or xylene) at 20-150°C. The reactions may be carried out under an inert gas (e.g. argon or nitrogen) to avoid water in order to obtain a preferable result.

The reaction of deprotection may be carried out by the same method as hereinbefore described.

In the compounds of the present invention of the formula (Ib), the compound in which at least one of A-J-E-, substituents of Ar in A, R^6 or R^7 in G, and -$COOR^2$ is -COOH or a group containing -COOH, or in which at least one of substituents of Ar in A, and R^6 or R^7 in G is amino, hydroxy or a group containing amino or hydroxy, that is the compound of the formula (Ib-2):

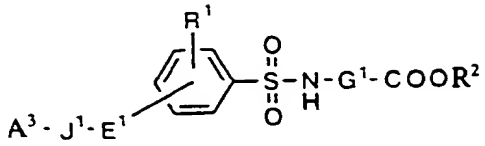


(Ib-2)

wherein G^2, E^2, J^2, and A^2 are as hereinbefore defined for G, E, J and A, with the proviso that at least one of A^2-J^2-E^2-, substituents of Ar in A^2, R^6 or R^7 in G^2, and -$COOR^2$ is -COOH or a group containing -COOH, or at least one of substituents of Ar in A^2, and R^6 or R^7 in G^2 is amino, hydroxy or a group containing amino or hydroxy, or A^2-J^2-E^2- is -CSOH, and the other symbols are as hereinbefore defined;
may be prepared by subjecting the compound of the formula (Ib-1) to deprotection.

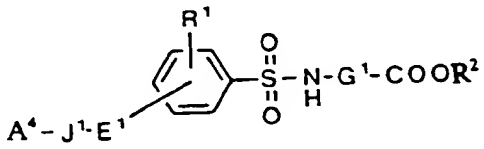
The reaction of deprotection may be carried out by the same method as hereinbefore described.
Besides, in the compounds of the present invention of the formula (Ib), the compound in which A represents Ar

substituted by at least one amino group, that is the compound of the formula (Ib-3):



(Ib-3)

wherein A^3 is as hereinbefore defined for Ar, with the proviso that A^3 is substituted by at least one amino group, and the other symbols are as hereinbefore defined: may be prepared by subjecting the compound prepared by the above methods of the formula (Ib-4):



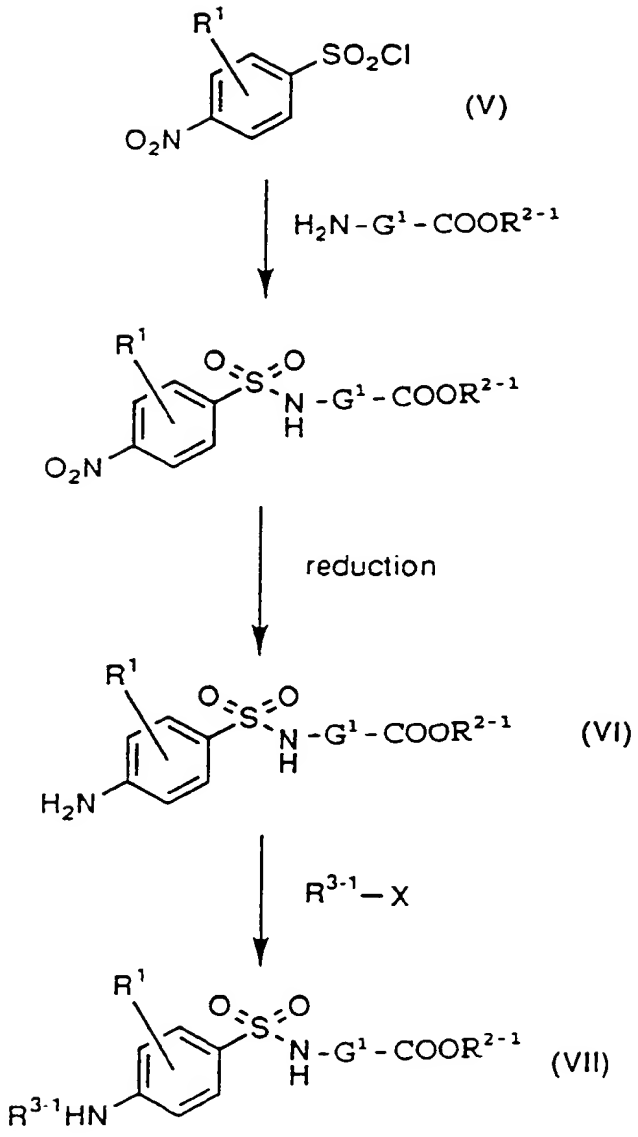
(Ib-4)

wherein A^4 is as hereinbefore defined for Ar, with the proviso that A^4 is substituted by at least one nitro group, and the other symbols are as hereinbefore defined: to hydrogenolysis.

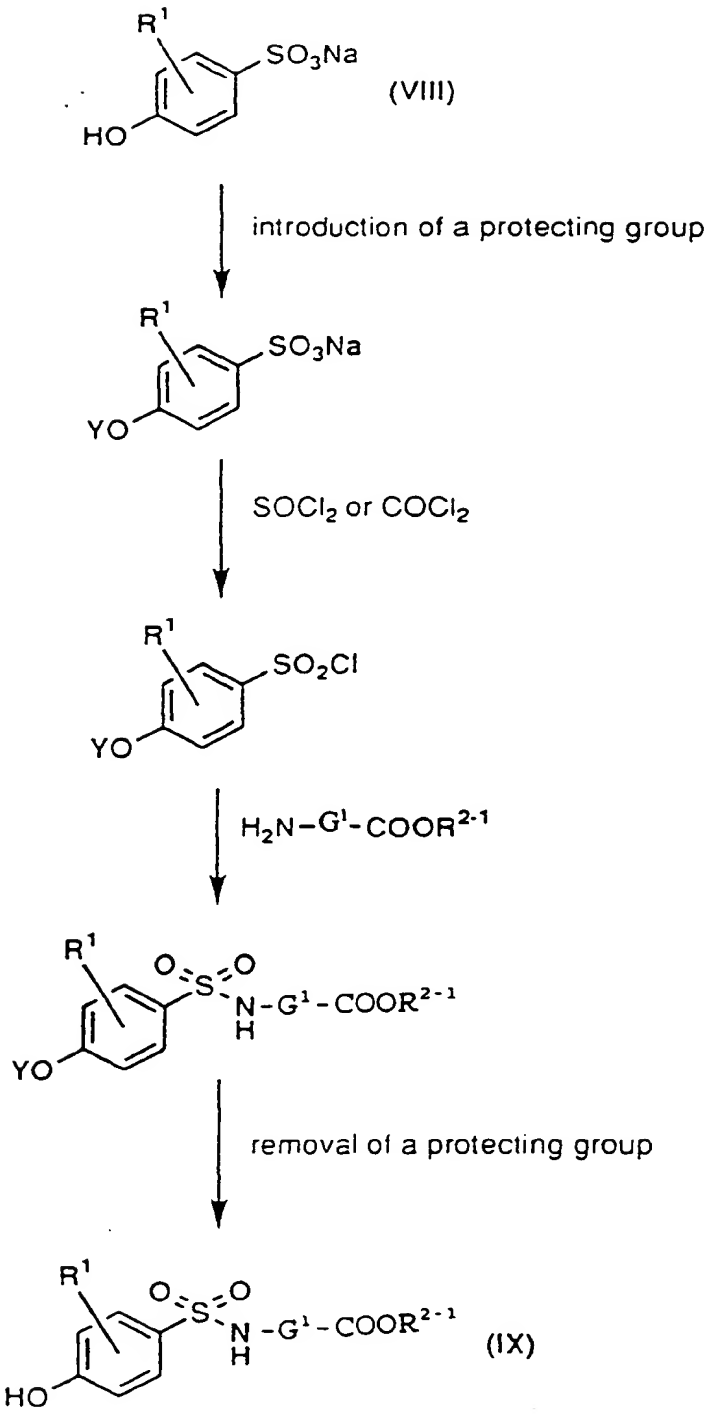
Hydrogenolysis may be carried out by the same method as hereinbefore described.

The compounds of formulae (IIb-a), (IIb-d), (IIb-f), (IIb-h), (IIb-j-1) and (IIb-j-2) may be prepared by known methods, methods described in the following schemes 1-3 or methods described in the Examples.

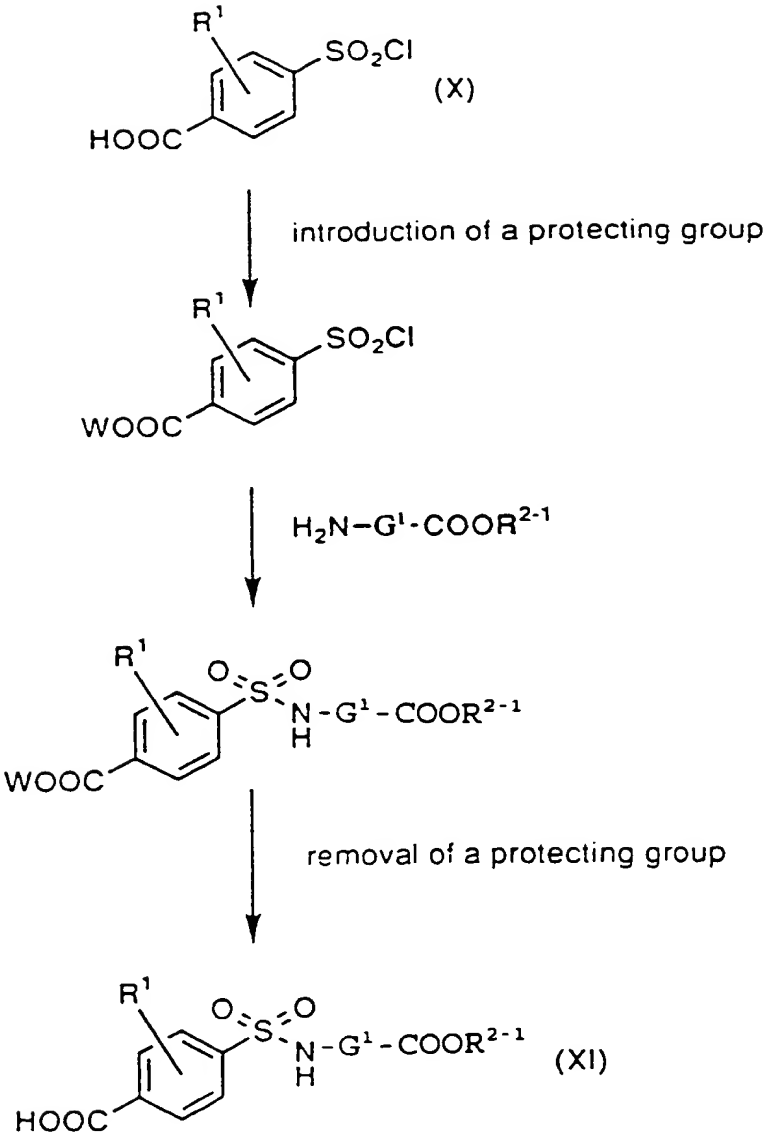
Scheme 1


R1
SO2Cl
O2N
(V)
H2N-G1-COOR2-1
R1
O
S
O
N
H
-G1-COOR2-1
O2N
reduction
R1
O
S
O
N
H
-G1-COOR2-1
(VI)
H2N
R3-1—X
R1
O
S
O
N
H
-G1-COOR2-1
(VII)
R3-1HN

Scheme 2


R1
SO3Na
HO
(VIII)
introduction of a protecting group
YO
SOCl2 or COCl2
SO2Cl
H2N-G1-COOR2-1
O
S
N
H
removal of a protecting group
(IX)

Scheme 3



In the above schemes, Y is a hydroxyl-protecting group (e.g. benzyl, benzyloxycarbonyl), W is a protecting group (e.g. benzyl, methyl) and the other symbols are as hereinbefore defined.

In the above schemes, the compounds of formulae (VI) and (VII) include compounds of the formula (IIb-a). The compound of the formula (IX) includes compounds of the formula (IIb-d). The compound of the formula (XI) includes compounds of the formula (IIb-f).

Each reaction in the above schemes may be carried out by a known method. In the above schemes, the compounds of formulae (V), (VIII) and (X) are known per se or may be prepared by known methods.

In each reaction in the present specification, products may be purified by conventional techniques. For example, purification may be carried out by distillation at atmospheric or reduced pressure, by high performance liquid chroma-

tography by thin layer chromatography or by column chromatography using silica gel or magnesium silicate, by washing or by recrystallization. Purification may be carried out after each reaction, or after a series of reactions.

The other starting materials and reagents in the present invention are known per se or may be prepared by known methods.

The potency of inhibitory activity of the compounds of formulae (Ia) and (Ib) against matrix metalloproteinases is confirmed as below. The IC_{50} value for inhibition of gelatinase A activity is determined as follows.

(1) Inhibitory activity against gelatinase A.

The progelatinase A (7µl: in assay buffer (90µl)) was purified from human normal skin dermal fibroblasts (HNDF). It was activated by the addition of 10mM p-aminophenylmercuric acetate (APMA) (10µl) for 1 hour at 37°C.

The solution of activated gelatinase A (7µl/tube. 98µl) was mixed with various concentrations of the test compound or dimethylsulfoxide (2µl) and gelatin (100µl) labeled with 0.05% fluorescein isothiocyanate (FITC) and incubated for 2 hours at 37°C. The reaction was terminated by the addition of 0.1M Tris-HCl (pH9.5) containing 94.7% ethanol (750µl). The mixture was stirred and then allowed to stand for 30 minutes at 0°C. The mixture was centrifuged for 30 minutes at 900 x g. The IC_{50} was determined by measuring the fluorescent intensity in supernatant (Ex=495nm, and Em=520nm). The results are shown in Table 24.

Table 24

Example No.	IC_{50} (µM)
2	0.11
2(10)	0.66
2(11)	0.80
2(35)	0.013
2(63)	0.0023
3(13)	0.0027
6	0.42
10(1)	0.70

The toxicity of the compounds of the present invention is very low and therefore the compounds may be considered safe for pharmaceutical use.

Inhibition of matrix metalloproteinase is useful for prevention and/or treatment of diseases induced by overexpression or excess activity of matrix metalloproteinases. for example, rheumatoid diseases, arthrosteitis, unusual bone resorption. osteoporosis, periodontitis, interstitial nephritis, arteriosclerosis, pulmonary emphysema, cirrhosis, cornea injury, metastasis, invasion or growth of tumor cells, autoimmune disease (e.g. Crohn's disease, Sjogren's syndrome), disease caused by vascular emigration or infiltration of leukocytes, arterialization in animals including human beings, especially human beings.

For the purpose above described, the compounds of formulae (Ia) or (Ib) of the present invention and non-toxic salts thereof (e.g. acid addition salts or hydrates) may normally be administered systemically or locally, usually by oral or parenteral administration.

The doses to be administered are determined depending upon, for example, age, body weight, symptom, the desired therapeutic effect, the route of administration, and the duration of the treatment. In the human adult, the doses per person are generally from 1 mg to 1000 mg, by oral administration, up to several times per day, and from 1 mg to 100 mg, by parenteral administration (preferably intravenous administration), up to several times per day, or continuous administration for from 1 to 24 hours per day from vein.

As mentioned above, the doses to be used depend upon various conditions. Therefore, there are cases in which doses lower than or greater than the ranges specified above may be used.

The compounds of the present invention may be administered in the form of, for example, solid compositions, liquid compositions or other compositions for oral administration, injections, liniments or suppositories for parenteral administration.

Solid compositions for oral administration include compressed tablets, pills, capsules, dispersible powders, and granules.

Capsules include hard capsules and soft capsules.

In such compositions, one or more of the active compound(s) may be admixed with at least one inert diluent (such

as lactose, mannitol, glucose, hydroxypropyl cellulose, microcrystalline cellulose, starch, polyvinylpyrrolidone or magnesium metasilicate aluminate). The compositions may also comprise, as is normal practice, additional substances other than inert diluents: e.g. lubricating agents (such as magnesium stearate), disintegrating agents (such as cellulose calcium glycolate), stabilizing agents, and agents to assist dissolution (such as glutamic acid or aspartic acid).

The tablets or pills may, if desired, be coated with a film of gastric or enteric material (such as sugar, gelatin, hydroxypropyl cellulose or hydroxypropylmethyl cellulose phthalate), or be coated with two or more films. And further, coating may include containment within capsules of absorbable materials such as gelatin.

Liquid compositions for oral administration include pharmaceutically acceptable emulsions, solutions, syrups and elixirs. In such compositions, one or more of the active compound(s) may be contained in an inert diluent(s) commonly used in the art (e.g purified water or ethanol). Besides inert diluents, such compositions may also comprise adjuvants (such as wetting agents or suspending agents), sweetening agents, flavouring agents, perfuming agents, and preserving agents.

Other compositions for oral administration include spray compositions which may be prepared by known methods and which comprise one or more of the active compound(s). Spray compositions may comprise additional substances other than inert diluents: e.g. stabilizing agents (such as sodium sulfate), isotonic buffers (such as sodium chloride, sodium citrate or citric acid). For preparation of such spray compositions, for example, the method described in the United States Patent No. 2,868,691 or 3,095,355 may be used.

Injections for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions and emulsions. Aqueous solutions and suspensions may include distilled water for injection or physiological salt solution. Non-aqueous solutions and suspensions may include propylene glycol, polyethylene glycol, vegetable oil such as olive oil, alcohol such as ethanol or POLYSORBATE80 (registered trade mark).

Injections may comprise additional ingredients other than inert diluents: e.g. preserving agents, wetting agents, emulsifying agents, dispersing agents, stabilizing agents, assisting agents such as agents to assist dissolution (e.g. glutamic acid or aspartic acid).

They may be sterilized for example, by filtration through a bacteria-retaining filter, by incorporation of sterilizing agents in the compositions or by irradiation. They may also be manufactured in the form of sterile solid compositions which may be dissolved in sterile water or some other sterile diluent(s) for injection immediately before use.

Other compositions for parenteral administration include liquids for external use, and endermic liniments, ointment, suppositories for rectal administration and pessaries for vaginal administration which comprise one or more of the active compound(s) and may be prepared by methods known per se.

Reference example and Example

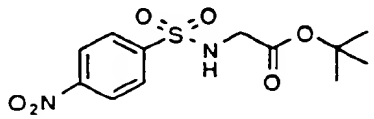
The following reference examples and examples illustrate the present invention, but do not limit the present invention.

The solvents in the parentheses show the developing or eluting solvents and the ratios of the solvents used are by volume in chromatographic separations or TLC.

The solvents in the parentheses in NMR show the solvents used in measurement.

Reference example 1

N-[(4-Nitrophenyl)sulfonyl]glycine t-butyl ester

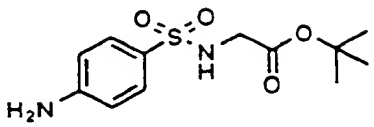


4-Nitrobenzenesulfonyl chloride (46.3 g) was added to a solution of glycine t-butyl ester hydrochloride (35 g) in pyridine (200 ml). The mixture was stirred for 1 hour at room temperature. The reaction mixture was concentrated. The precipitated crystals was washed with water and then a mixture of hexane and ethyl acetate (9 : 1) and dried to give the title compound (61.4 g) having the following physical data.

TLC: Rf 0.18 (Hexane : Ethyl acetate = 4 : 1).

Reference example 2

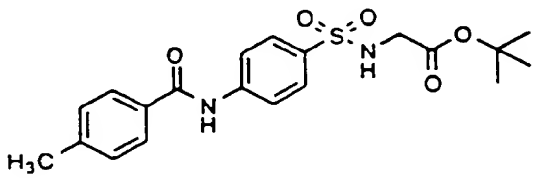
N-[(4-Aminophenyl)sulfonyl]glycine t-butyl ester



To a solution of the compound prepared in reference example 1 (57.1 g) in ethanol (200 ml) and tetrahydrofuran (200 ml), 10% palladium carbon (2.2 g) was added. The mixture was stirred for 3 hours at room temperature under an atmosphere of hydrogen. The reaction mixture was filtered through celite (registered trade mark). The filtrate was concentrated. The precipitated crystals was washed with a mixture of hexane and ethyl acetate (4 : 1) and dried to give the title compound (50 g) having the following physical data.
TLC: Rf 0.36 (Hexane : Ethyl acetate = 1 : 1).

Example 1

N-[[4-(p-Toluoylamino)phenyl]sulfonyl]glycine t-butyl ester



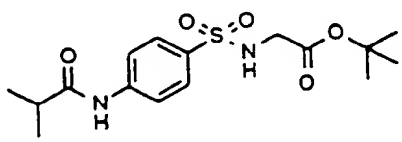
To a solution of the compound prepared in reference example 2 (1.2 g) in pyridine (10 ml), p-toluoyl chloride (0.5 ml) was added at 0°C. The mixture was stirred for 30 minutes at room temperature. To the reaction mixture, 1N hydrochloric acid (100 ml) was added. The mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous solution of sodium bicarbonate, a saturated aqueous solution of sodium chloride, dried over anhydrous sodium sulfate and concentrated. The residue was washed with ether and dried to give the title compound (1.52 g) having the following physical data.
TLC: Rf 0.56 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$):δ 8.08-8.00 (1H, br.s), 7.86 (2H, d, J=9.2Hz), 7.82 (2H, d, J=9.2Hz), 7.78 (2H, d, J=8.2Hz), 7.31 (2H, d, J=8.2Hz), 5.04 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.44 (3H, s), 1.37 (9H, s).

Example 1(1)-1(91)

The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 1, using a corresponding acyl chloride instead of p-toluoyl chloride.

Example 1(1)

N-[[4-(Isobutyrylamino)phenyl]sulfonyl]glycine t-butyl ester

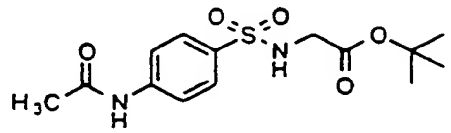


TLC: Rf 0.41 (Hexane : Ethyl acetate = 1:1).

NMR ($CDCl_3$): δ 7.77 (2H, d, J=9.0Hz), 7.68 (2H, d, J=9.0Hz), 5.15 (1H, t, J=5.4Hz), 3.64 (2H, d, J=5.4Hz), 2.56 (1H, m), 1.36 (9H, s), 1.25 (6H, d, J=6.8Hz).

Example 1(2)

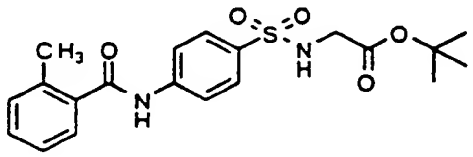
N-[[4-(Acetylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.36 (Hexane : Ethyl acetate = 3 : 7).
NMR ($CDCl_3$): δ 7.78 (2H, d, J=8.8Hz), 7.76-7.72 (1H), 7.65 (2H, d, J=8.8Hz), 5.11(1H, t, J=5.4Hz), 3.65 (2H, d, J=5.4Hz), 2.21 (3H, s), 1.36 (9H, s).

Example 1(3)

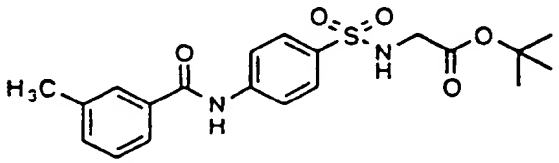
N-[[4-(o-Toluoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.64 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 7.83 (2H, d, J=8.8Hz), 7.76 (2H, d, J=8.8Hz), 7.88-7.72 (1H), 7.52-7.22 (4H, m), 5.01 (1H, t, J=5.4Hz), 3.65 (2H, d, J=5.4Hz), 2.49 (3H, s), 1.37 (9H, s).

Example 1(4)

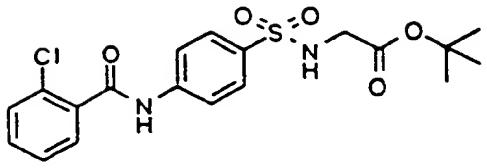
N-[[4-(m-Toluoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.59 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 8.10-8.04 (1H, br.s), 7.85 (2H, d, J=9.2Hz), 7.80 (2H, d, J=9.2Hz), 7.72-7.60 (2H, m), 7.43-7.36 (2H, m), 5.05 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.44 (3H, s), 1.37 (9H, s).

Example 1(5)

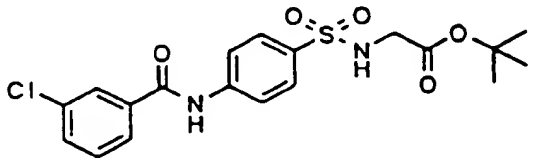
N-[[4-(2-Chlorobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC. Rf 0.52 (Hexane : Ethyl acetate = 1 : 1),
NMR($CDCl_3$). δ 8.22-8.12 (1H, br.s), 7.87 (2H. d. J=8.6Hz), 7.84-7.74 (1H, m), 7.79 (2H. d. J=8.6Hz). 7.50-7.36 (3H. m), 5.03 (1H. t. J=5.6Hz). 3.67 (2H, d. J=5.6Hz), 1.36 (9H. s).

Example 1(6)

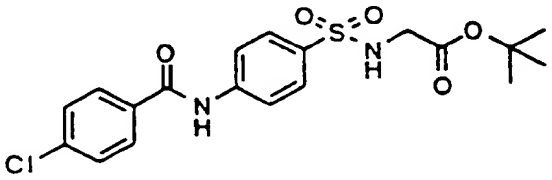
N-[[4-(3-Chlorobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.58 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.02-7.94 (1H, br.s), 7.92-7.72 (6H, m), 7.61-7.40 (2H, m), 5.02 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 1.37 (9H. s).

Example 1(7)

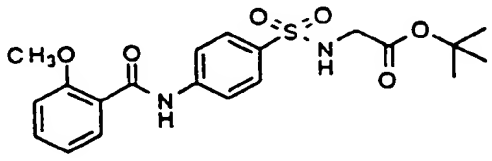
N-[[4-(4-Chlorobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.64 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.00-7.90 (1H, br.s), 7.87 (2H, d. J=8.6Hz), 7.83 (2H, d, J=8.8Hz), 7.78 (2H, d, J=8.6Hz), 7.49 (2H, d. J=8.8Hz). 5.00 (1H, t, J=5.4Hz), 3.67 (2H, d. J=5.4Hz), 1.37 (9H, s).

Example 1(8)

N-[[4-(2-Methoxybenzoylamino)phenyl]sulfonyl]glycine t-butyl ester

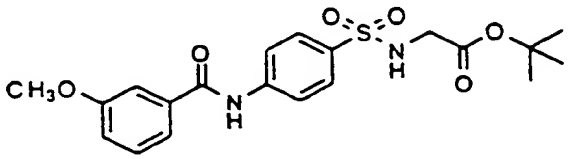


TLC: Rf 0.42 (Hexane : Ethyl acetate = 1 : 1),
NMR($CDCl_3$): δ 10.08-10.00 (1H, br.s), 8.28 (1H, dd, J=2.0, 8.0Hz), 7.87 (2H, d, J=9.4Hz), 7.82 (2H, d, J=9.4Hz),

7.60-7.48 (1H, m), 7.21-7.11 (1H, m), 7.06 (1H, d, J=8.4Hz), 4.99 (1H, t, J=5.4Hz), 4.09 (3H, s), 3.67 (2H, d, J=5.4Hz), 1.36 (9H, s).

Example 1(9)

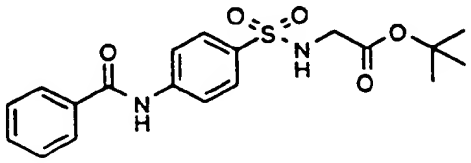
N-[[4-(3-Methoxybenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.52 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.02-7.96 (1H, br.s), 7.87 (2H, d, J=9.2Hz), 7.80 (2H, d, J=9.2Hz), 7.47-7.36 (3H, m), 7.15-7.08 (1H, m), 5.01 (1H, t, J=5.4Hz), 3.88 (3H, s), 3.68 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(10)

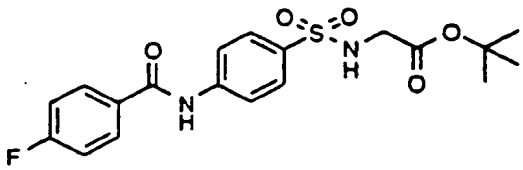
N-[[4-(Benzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.70 (Ethyl acetate),
NMR ($CDCl_3$): δ 8.02 (1H, s), 7.9-7.8 (6H, m), 7.6-7.3 (3H, m), 5.02 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(11)

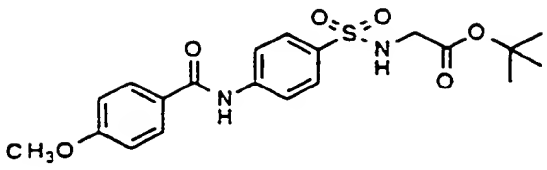
N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.53 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$+CD_3OD): δ 7.88 (2H, dd, J=5.2, 8.8Hz), 7.82-7.75 (4H, m), 7.11 (2H, t, J=8.8Hz), 3.60 (2H, s), 1.31 (9H, s).

Example 1(12)

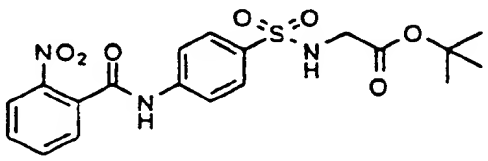
N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC. Rf 0.40 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$). δ 7.94-7.90 (1H, br.s), 7.86 (2H, d, J=9.2Hz), 7.85 (2H, d, J=8.8Hz), 7.79 (2H, d, J=9.2Hz), 6.99 (2H, d, J=8.8Hz), 5.00 (1H, t, J=5.4Hz), 3.89 (3H, s), 3.67 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(13)

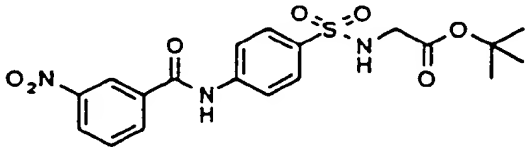
N-[[4-(2-Nitrobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.62 (Ethyl acetate),
NMR (CD_3OD): δ 8.19 (1H, d, J=8.4Hz), 7.9-7.7 (7H, m), 3.65 (2H, s), 1.35 (9H, s).

Example 1(14)

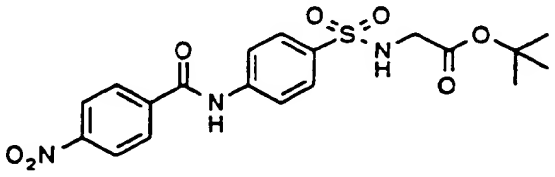
N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.72 (Ethyl acetate),
NMR ($CDCl_3$+CD_3OD): δ 8.85 (1H, s), 8.43 (1H, d, J=8.0Hz), 8.35 (1H, d, J=8.0Hz), 7.94 (2H, d, J=8.8Hz), 7.85 (2H, d, J=8.8Hz), 7.73 (1H, t, J=8.0Hz), 3.68 (2H, s), 1.38 (9H, s).

Example 1(15)

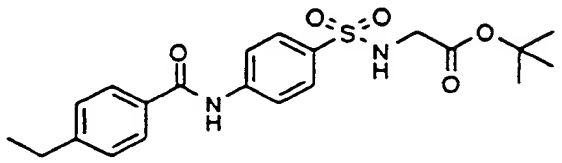
N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.74 (Ethyl acetate),
NMR (DMSO-d6): δ 10.88 (1H, s), 8.39 (2H, d, J=8.8Hz), 8.20 (2H, d, J=8.8Hz), 8.01 (1H, t, J=6.0Hz), 7.97 (2H, d, J=8.8Hz), 7.79 (2H, d, J=8.8Hz), 3.58 (2H, d, J=6.0Hz), 1.32 (9H, s).

Example 1(16)

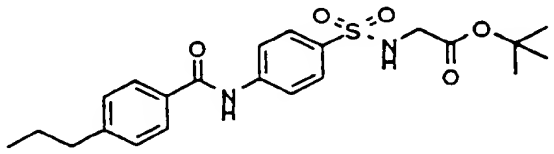
N-[[4-(4-Ethylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC Rf 0.56 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.00-7.98 (1H, br.s), 7.87 (2H, d, J=8.4Hz), 7.81 (2H, d, J=8.4Hz), 7.80 (2H, d, J=8.2Hz), 7.34 (2H, d, J=8.2Hz), 5.00 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.74 (2H, q, J=7.4Hz), 1.37 (9H, s),1.28 (3H, t, J=7.4Hz).

Example 1(17)

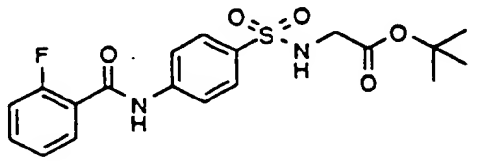
N-[[4-(4-Propylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.62 (Hexane : Ethyl acetate = 1 : 1),
NMR($CDCl_3$): δ 8.02-7.95 (1H, br.s), 7.86 (2H, d, J=8.8Hz), 7.81 (2H, d, J=8.8Hz), 7.80 (2H, d, J=8.4Hz), 7.31 (2H, d, J=8.4Hz), 5.01 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.67 (2H, t, J=7.4Hz), 1.80-1.60 (2H, m), 1.37 (9H, s), 0.96 (3H, t, J=7.4Hz).

Example 1(18)

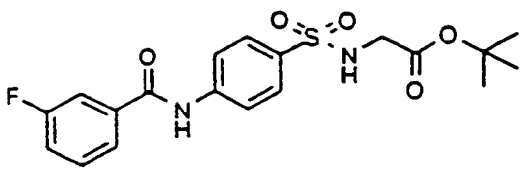
N-[[4-(2-Fluorobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.53 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 8.65 (1H, br.s), 8.18 (1H, dt, J=2.0, 8.0Hz), 7.88 (2H, d, J=8.8Hz), 7.83 (2H, d, J=8.8Hz), 7.64-7.51 (1H, m), 7.35 (1H, dt, J=1.0, 7.4Hz), 7.28-7.15 (1H, m), 5.02 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 1.36 (9H, s).

Example 1(19)

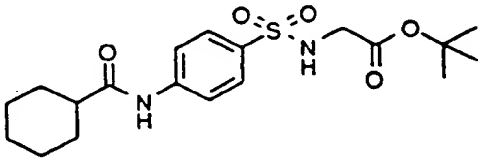
N-[[4-(3-Fluorobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC Rf 0.53 (Hexane . Ethyl acetate = 1 : 1).
NMR ($CDCl_3$) δ 8.00-7 93 (1H, br.s), 7.88 (2H, d, J=8.8Hz), 7.80 (2H, d, J=8.8Hz), 7.68-7 44 (3H, m), 7.35-7.27 (1H, m), 5.01 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(20)

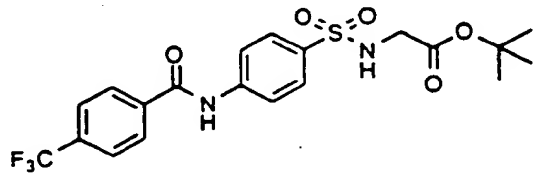
N-[[4-(Cyclohexylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.55 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 7.80 (2H, d, J=8.8Hz), 7.68 (2H, d, J=8.8Hz), 7.44-7.32 (1H, br.s), 5.00 (1H, t, J=5.0Hz), 3.65 (2H, d, J=5.0Hz), 2.35-2.18 (1H, m), 2.04-1.20 (10H, m), 1.36 (9H, s).

Example 1(21)

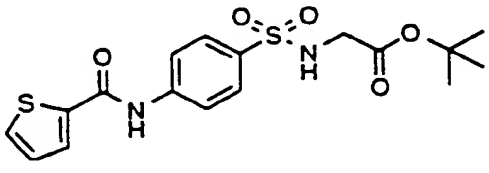
N-[[4-(4-Trifluoromethylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.65 (Hexane : Ethyl acetate = 1 : 1),
NMR (DMSO-d6): δ 10.83 (1H, s), 8.18 (2H, d, J=8.0Hz), 8.04-7.95 (1H), 7.98 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.0Hz), 7.77 (2H, d, J=8.8Hz), 3.55 (2H, d, J=6.2Hz), 1.32 (9H, s).

Example 1(22)

N-[[4-(2-Thienylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester

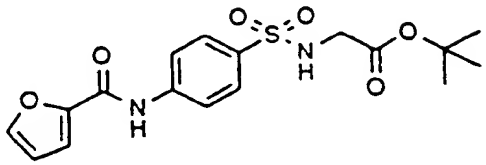


TLC: Rf 0.26 (Hexane : Ethyl acetate = 1 : 1),
NMR($CDCl_3$): δ 7.95 (1H, s), 7.84 (2H, d, J=8.8Hz), 7.77 (2H, d, J=8.8Hz), 7.68 (1H, dd, J=1.0, 3.8Hz), 7.61 (1H, dd,

J=1.0, 4.8Hz), 7.16 (1H, dd, J=3.8, 4.8Hz), 5.05 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 1.37 (9H, S).

Example 1(23)

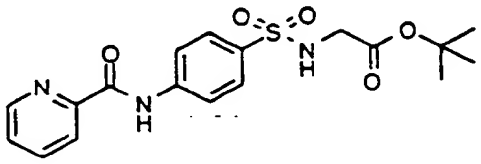
N-[[4-(2-Furylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.19 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.25 (1H, s), 7.86-7.82 (4H, m), 7.55 (1H, d, J=1.8Hz), 7.30 (1H, d, J=3.6Hz), 6.60 (1H, dd, J=1.8, 3.6Hz), 5.03 (1H, t, J=5.6Hz), 3.68 (2H, d, J=5.6Hz), 1.36 (9H, s).

Example 1(24)

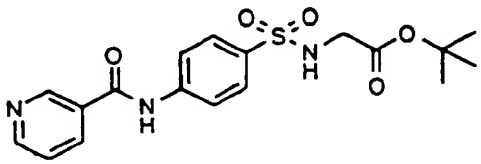
N-[[4-(2-Pyridylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.45 (Hexane : Ethyl acetate = 1 : 1),
NMR($CDCl_3$): δ 10.33-10.20 (1H, br.s), 8.64-8.60 (1H, m), 8.31 (1H, d, J=7.8Hz), 8.00-7.85 (1H, m), 7.95 (2H, d, J=9.0Hz), 7.88 (2H, d, J=9.0Hz), 7.53 (1H, m), 5.02 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 1.36 (9H, s).

Example 1(25)

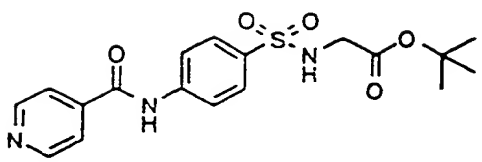
N-[[4-(3-Pyridylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.40 (Ethyl acetate),
NMR ($CDCl_3$): δ 9.11 (1H, br.s), 8.81 (1H, dd, J=1.6, 4.8Hz), 8.27-8.20 (1H, m), 8.20-8.10 (1H, br.s), 7.88 (2H, d, J=9.0Hz), 7.81 (2H, d, J=9.0Hz), 7.53-7.44 (1H, m), 5.10 (1H, t, J=5.4Hz), 3.69 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(26)

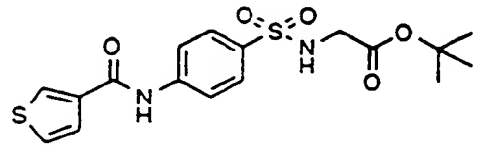
N-[[4-(4-Pyridylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC Rf 0.36 (Ethyl acetate).
NMR ($CDCl_3$ + CD_3OD(10 drops)): δ 8.76-8.71 (2H, m), 7.93 (2H, d, J=9.0Hz), 7.89-7.82 (2H, m), 7.85 (2H, d, J=9.0Hz), 3.66 (2H, s), 1.37 (9H, s).

Example 1(27)

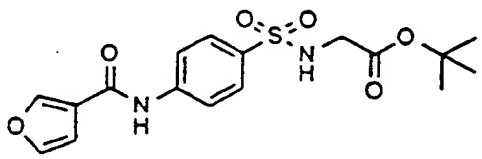
N-[[4-(3-Thienylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC Rf 0.27 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$ + CD_3OD): δ 8.16 (1H, m), 7.87 (2H, d, J=9.0Hz), 7.82 (2H, d, J=9.0Hz), 7.61 (1H, m), 7.40 (1H, m), 3.66 (2H, s), 1.36 (9H, s).

Example 1(28)

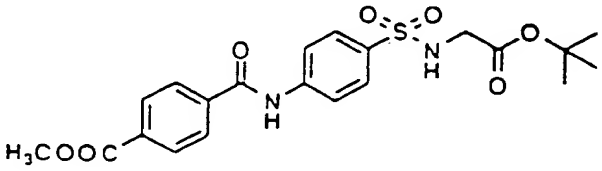
N-[[4-(3-Furylcarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.29 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$ + CD_3OD): δ 8.17 (1H, m), 7.84 (2H, d, J=9.0Hz), 7.82 (2H, d, J=9.0Hz), 7.49 (1H, m), 6.88 (1H, m), 3.66 (2H, s), 1.37 (9H, s).

Example 1(29)

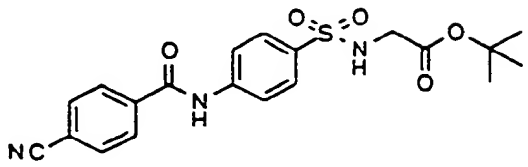
N-[[4-(4-Methoxycarbonylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.43 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.05-7.98 (1H, br.s), 7.94 (2H, d, J=8.4Hz), 7.89 (2H, d, J=9.0Hz), 7.82 (2H, d, J=9.0Hz), 5.01 (1H, t, J=5.4Hz), 3.97 (3H, s), 3.69 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(30)

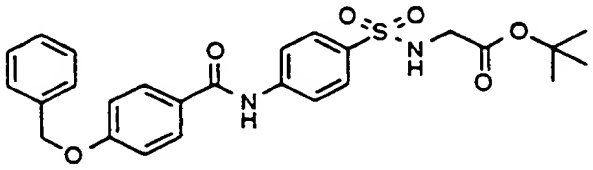
N-[[4-(4-Cyanobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.41 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 8.15 (1H, s), 8.00 (2H, d, J=8.2Hz), 7.85 (2H, d, J=9.0Hz), 7.80 (2H, d, J=8.2Hz), 7.79 (2H, d, J=9.0Hz), 5.06 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(31)

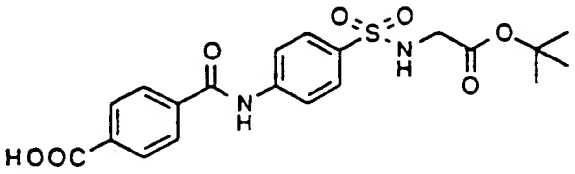
N-[[4-(4-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.58 (Hexane : Ethyl acetate = 1 : 1),
NMR(DMSO-d6): δ 10.41 (1H, s), 8.04-7.88(1H, s), 7.97 (2H, d, J=8.4Hz), 7.96 (2H, d, J=8.4Hz), 7.74 (2H, d, J=8.4Hz), 7.52-7.28 (5H, m), 7.16 (2H, d, J=8.4Hz), 5.21 (2H, s), 3.56 (2H, s), 1.32 (9H, s).

Example 1(32)

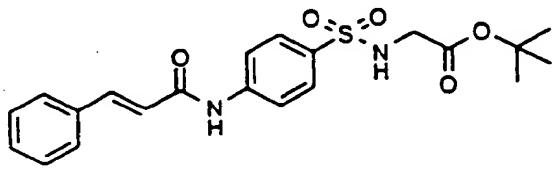
N-[[4-(4-Carboxybenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



The title compound was not measured the physical data and was used for the next step.

Example 1(33)

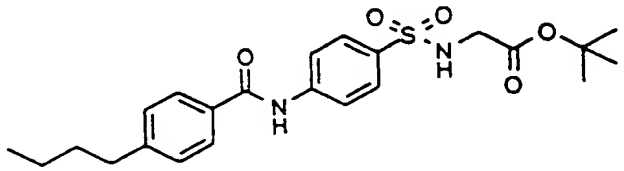
N-[[4-(Cinnamoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.50 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 7.85 (2H, d, J=8.8Hz), 7.79 (1H, d, J=15.6Hz), 7.77 (2H, d, J=8.8Hz), 7.65-7.50 (3H, m), 7.46-7.38 (3H, m), 6.56 (1H, d, J=15.6Hz), 5.03 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 1.36 (9H, s).

Example 1(34)

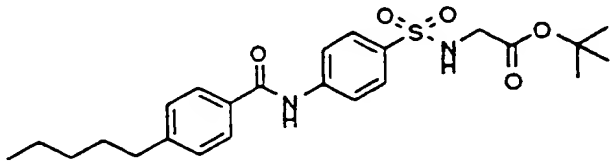
N-[[4-[(4-Butylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.27 (Hexane : Ethyl acetate = 7 : 3),
NMR ($CDCl_3$): δ 7.97 (1H, s), 7.87 (2H, d, J=9.0Hz), 7.80 (2H, d, J=9.0Hz), 7.79 (2H, d, J=8.0Hz), 7.32 (2H, d, J=8.0Hz), 5.01 (1H, t, J=5.4Hz), 3.68 (2H, d, J=5.4Hz), 2.69 (2H, t, J=7.4Hz), 1.70-1.50 (2H, m), 1.45-1.20 (2H, m), 1.37 (9H, s), 0.94 (3H, t, J=7.2Hz).

Example 1(35)

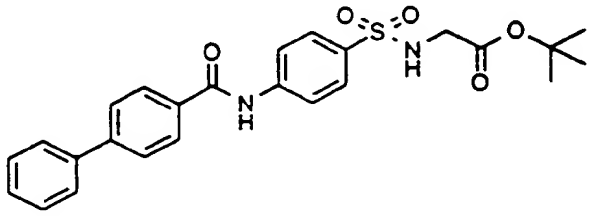
N-[[4-(4-Pentylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.28 (Hexane : Ethyl acetate = 7 : 3),
NMR ($CDCl_3$): δ 7.99 (1H, s), 7.86 (2H, d, J=9.0Hz), 7.80 (2H, d, J=9.0Hz), 7.79 (2H, d, J=8.2Hz), 7.31 (2H, d, J=8.2Hz), 5.02 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.68 (2H, t, J=7.4Hz), 1.72-1.50 (2H, m), 1.45-1.20 (4H, m), 1.36 (9H, s), 0.89 (3H, t, J=6.6Hz).

Example 1(36)

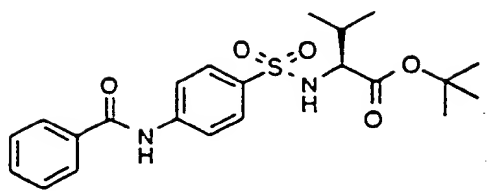
N-[[4-(4-Phenylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.67 (Hexane : Ethyl acetate = 1 : 1),
NMR (DMSO-d6): δ 10.61 (1H, s), 8.08 (2H, d, J=8.4Hz), 8.04-7.93 (1H, m), 8.00 (2H, d, J=9.0Hz), 7.85 (2H, d, J=8.4Hz), 7.82-7.72 (2H), 7.77 (2H, d, J=9.0Hz), 7.58-7.36 (3H, m), 3.57 (2H, d, J=6.4Hz), 1.32 (9H, s).

Example 1(37)

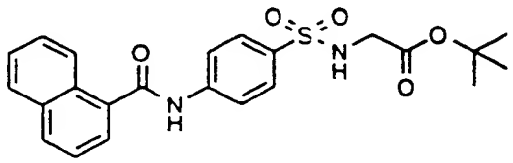
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-valine t-butyl ester



TLC. Rf 0.39 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.02 (1H. s), 7.9-7.75 (6H. m). 7.65-7.45 (3H. m). 5.14 (1H. d. J=9.9Hz). 3.66 (1H. dd. J=4.4. 9.9Hz), 2.05 (1H. m). 1.26 (9H. s), 1.00 (3H. d. J=7.0Hz). 0.85 (3H. d. J=7.0Hz).

Example 1(38)

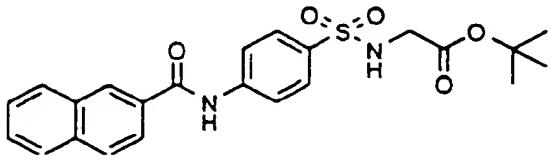
N-[[4-(1-Naphthoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.57 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.34-8.24 (1H. m), 8.10 (1H, s), 7.98 (1H, d, J=8.0Hz), 7.94-7.85 (1H, m), 7.85-7.76 (4H, m), 7.72 (1H. dd. J=1.2. 7.2Hz), 7.64-7.51 (2H. m), 7.47 (1H, d, J=7.2Hz), 5.03 (1H, t, J=5.4Hz), 3.65 (2H. d. J=5.4Hz), 1.38 (9H. s).

Example 1(39)

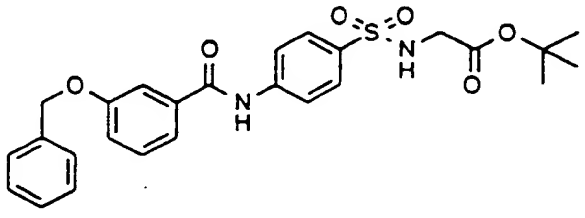
N-[[4-(2-Naphthoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.57 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.40 (1H, d, J=0.8Hz), 8.23 (1H. s), 8.02-7.80 (8H, m), 7.68-7.54 (2H, m), 5.03 (1H, t. J=5.2Hz), 3.68 (2H. d. J=5.2Hz). 1.38 (9H, s).

Example 1(40)

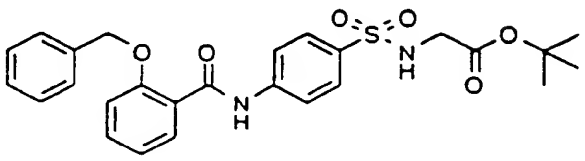
N-[[4-(3-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.49 Hexane Ethyl acetate = 1 : 1).
NMR ($CDCl_3$) δ 7.95 (1H, s), 7.87 (2H, d, J=9.0Hz), 7.78 (2H, d, J=9.0Hz), 7.54-7.32 (6H, m), 7.24-7.15 (1H, m),5.14 (2H, s), 5.00 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(41)

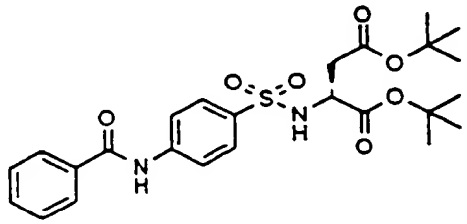
N-[[4-(2-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.53 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 10.25 (1H, s), 8.32 (1H, d, J=7.8Hz), 7.66 (2H, d, J=8.8Hz), 7.62-7.47 (5H, m), 7.32-7.22 (1H, m), 7.27 (2H, d, J=8.8Hz), 7.17 (2H, m), 5.23 (2H, s), 4.94 (1H, t, J=5.4Hz), 3.62 (2H, d, J=5.4Hz), 1.34 (9H, s).

Example 1(42)

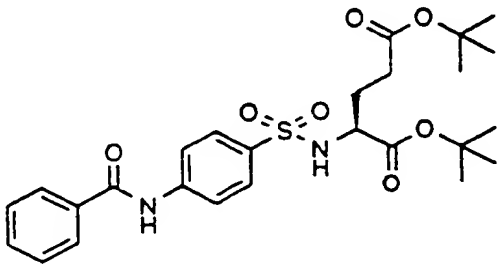
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-aspartic acid di-t-butyl ester



TLC: Rf 0.46 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.02 (1H, s), 7.90-7.75 (6H, m), 7.65-7.45 (3H, m), 5.63 (1H, d, J=8.2Hz), 4.00 (1H, m), 2.82 (1H, dd, J=4.6, 16.8Hz), 2.72 (1H, dd, J=4.8, 16.8Hz), 1.44 (9H, s), 1.33 (9H, s).

Example 1(43)

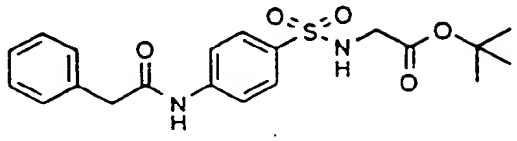
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-glutamic acid di-t-butyl ester



TLC: Rf 0.42 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.08 (1H, s), 7.9-7.8 (6H, m), 7.65-7.25 (3H, m), 5.26 (1H, d, J=9.4Hz), 3.83 (1H, m), 2.40 (2H, m), 2.15-1.65 (2H, m), 1.46 (9H, s), 1.28 (9H, s).

Example 1(44)

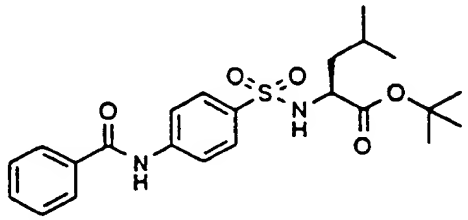
N-[[4-(Phenylacetylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.41 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 7.75 (2H, d, J=8.8Hz), 7.57 (2H, d, J=8.8Hz), 7.48-7.29 (6H, m), 5.03 (1H, t, J=5.4Hz), 3.76 (2H, s), 3.63 (2H, d, J=5.4Hz), 1.35 (9H, s).

Example 1(45)

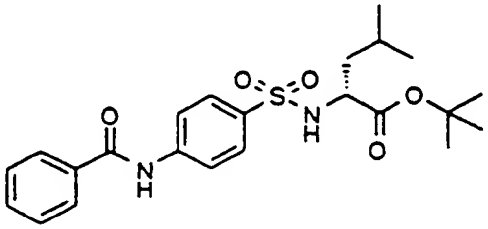
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-leucine t-butyl ester



TLC: Rf 0.45 (Hexane . Ethyl acetate = 1 : 1),
NMR (DMSO-d6): δ 10.29 (1H, s), 8.2-8.05 (1H), 7.96 (2H, dd, J=1.6,8.2Hz), 7.72 (2H, d, J=8.8Hz), 7.6-7.45 (5H, m), 3.86 (1H, m), 1.8-1.5 (3H, m), 1.46 (9H, s), 0.91 (3H, d, J=6.2Hz), 0.90 (3H, d, J=6.2Hz).

Example 1(46)

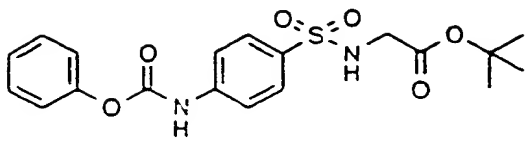
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-leucine t-butyl ester



TLC: Rf 0.45 (Hexane : Ethyl acetate = 1 : 1),
NMR (DMSO-d6): δ 10.29 (1H, s), 8.2-8.05 (1H), 7.96 (2H, dd, J=1.6, 8.0Hz), 7.72 (2H, d, J=8.8Hz), 7.6-7.45 (5H, m), 3.86 (1H, m), 1.8-1.5 (3H, m), 1.46 (9H, s), 0.91 (3H, d, J=6.2Hz), 0.90 (3H, d, J=6.2Hz).

Example 1(47)

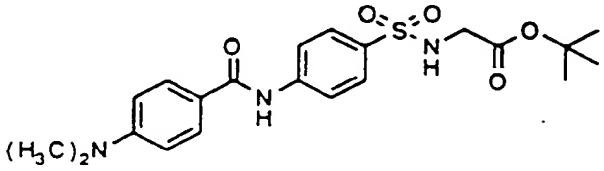
N-[[4-(Phenoxycarbonylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC. Rf 0.55 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 7.84 (2H, d, J=8.8Hz), 7.59 (2H, d, J=8.8Hz), 7.48-7.36 (2H, m), 7.33-7.16 (4H, m), 5.01 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 1(48)

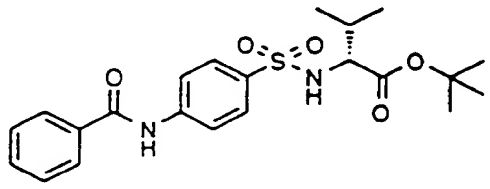
N-[[4-(4-Dimethylaminobenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC. Rf 0.23 (Hexane : Ethyl acetate = 1 : 1).
NMR (DMSO-d6): δ 10.18 (1H, s), 8.0-7.85 (5H, m), 7.72 (2H, d, J=8.8Hz), 6.77 (2H, d, J=9.0Hz), 3.56 (2H, d, J=6.0Hz), 3.01 (6H, s), 1.32 (9H, s).

Example 1(49)

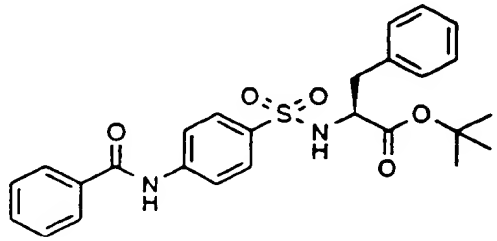
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-valine t-butyl ester



TLC: Rf 0.43 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 7.99 (1H, s), 7.9-7.75 (6H, m), 7.6-7.45 (3H, m), 5.13 (1H, d, J=9.8Hz), 3.65 (1H, dd, J=4.4, 9.8Hz), 2.05 (1H, m), 1.26 (9H, s), 1.00 (3H, d, J=6.8Hz), 0.85 (3H, d, J=6.8Hz).

Example 1(50)

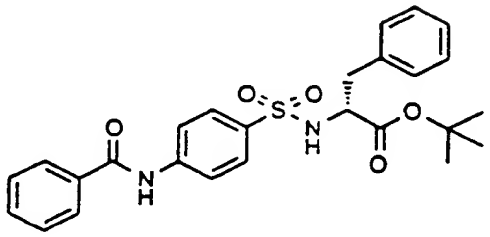
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-Phenylalanine t-butyl ester



TLC: Rf 0.44 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 8.02 (1H, s), 7.87 (2H, m), 7.76 (4H, s), 7.65-7.45 (3H, m), 7.3-7.1 (5H, m), 5.13 (1H, d, J=9.0Hz), 4.10 (1H, dt, J=9.0, 6.0Hz), 3.03 (2H, d, J=6.0Hz), 1.23 (9H, s).

Example 1(51)

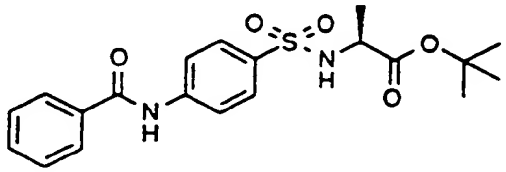
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-Phenylalanine t-butyl ester



TLC: Rf 0.44 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 7.98 (1H, s), 7.88 (2H, m), 7.76 (4H, s), 7.65-7.45 (3H, m), 7.3-7.1 (5H, m), 5.11 (1H, d, J=9.2Hz), 4.10 (1H, dt, J=9.2, 6.0Hz), 3.03 (2H, d, J=6.0Hz), 1.23 (9H, s).

Example 1(52)

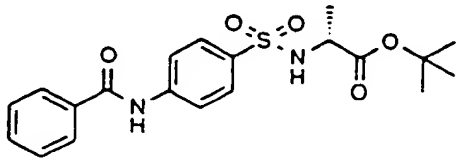
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-alanine di-t-butyl ester



TLC: Rf 0.37 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.15 (1H, br.s), 7.89 (2H, dd, J=1.6, 8.4Hz), 7.81 (4H, s), 7.65-7.45 (3H, m), 5.30 (1H, br.d, J=8.2Hz), 3.86 (1H, m), 1.36 (3H, d, J=7.2Hz), 1.32 (9H, s).

Example 1(53)

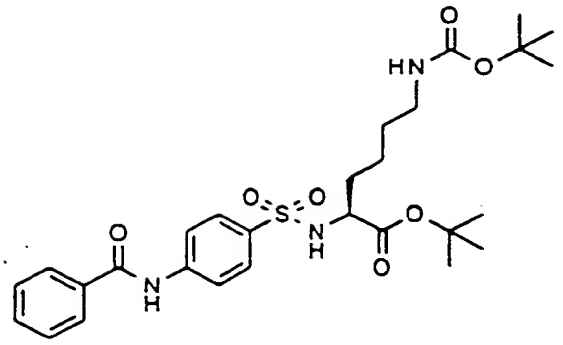
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-alanine t-butyl ester



TLC: Rf 0.37 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.10 (1H, br.s), 7.88 (2H, dd, J=1.6, 8.4Hz), 7.81 (4H, s), 7.65-7.45 (3H, m), 5.28 (1H, d, J=8.2Hz), 3.86 (1H, m), 1.36 (3H, d, J=7.0Hz), 1.32 (9H, s).

Example 1(54)

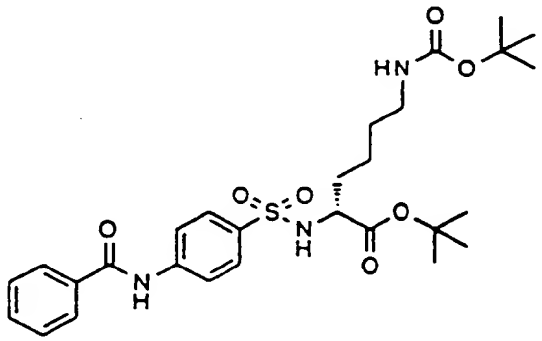
N-[[4-(Benzoylamino)phenyl]sulfonyl]-t-buloxycarbonyl-L-lysine t-butyl ester



TLC: Rf 0.26 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.13 (1H, br.s), 7.91 (2H, m), 7.83 (4H, s), 7.65-7.45 (3H, m), 5.23 (1H, d, J=9.0Hz), 4.38 (1H, m), 3.79 (1H, m), 3.03 (2H, m), 1.9-1.3 (6H, m), 1.44 (9H, s), 1.30 (9H, s).

Example 1(55)

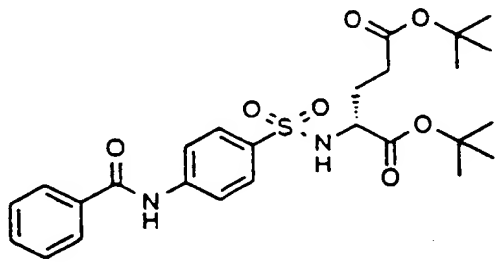
N-[[4-(Benzoylamino)phenyl]sulfonyl]-t-butoxycarbonyl-D-lysine t-butyl ester



TLC: Rf 0.28 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.19 (1H, br.s), 7.91 (2H, m), 7.85 (2H, d, J=8.8Hz), 7.80 (2H, d, J=8.8Hz), 7.65-7.45 (3H, m), 5.22 (1H, d, J=8.8Hz), 4.57 (1H, m), 3.79 (1H, m), 3.03 (2H, m), 1.90-1.25 (6H, m), 1.44 (9H, s), 1.30 (9H, s).

Example 1(56)

N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-glulamic acid di-t-butyl ester

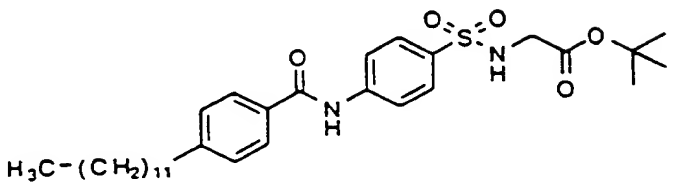


TLC: Rf 0.41 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.11 (1H, s), 7.88 (2H, d, J=8.4Hz), 7.81 (4H, s), 7.65-7.45 (3H, m), 5.26 (1H, d, J=9.0Hz), 3.82 (1H,

m). 2.4 (2H, m), 2.05 (1H, m), 1.79 (1H, m), 1.46 (9H, s), 1.28 (9H, s).

Example 1(57)

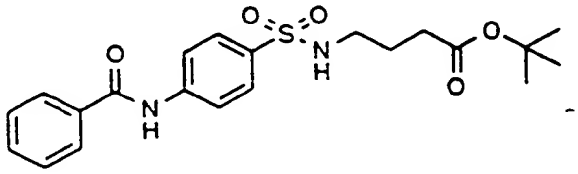
N-[[4-(4-Dodecylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.33 (Hexane : Ethyl acetate = 7 : 3),
NMR ($CDCl_3$): δ 7.98 (1H, s), 7.86 (2H, d, J=9.0Hz), 7.80 (2H, d, J=9.0Hz), 7.79 (2H, d, J=8.4Hz), 7.31 (2H, d, J=8.4Hz), 5.01 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.86 (2H, t, J=7.4Hz), 1.74-1.50 (2H, m), 1.37 (9H, s), 1.36-1.10 (18H, m), 0.88 (3H, t, J=6.8Hz).

Example 1(58)

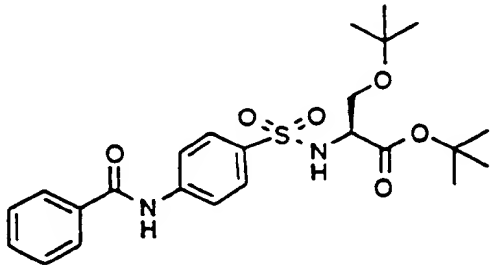
4-[N-[[4-(Benzoylamino)phenyl]sulfonyl]amino]butyric acid t-butyl ester



TLC: Rf 0.31 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.09 (1H, s), 7.9-7.75 (6H, m), 7.65-7.45 (3H, m), 4.80 (1H, t, J=6.4Hz), 3.00 (2H, q, J=6.4Hz), 2.27 (2H, t, J=6.8Hz), 1.76 (2H, m), 1.43 (9H, s).

Example 1(59)

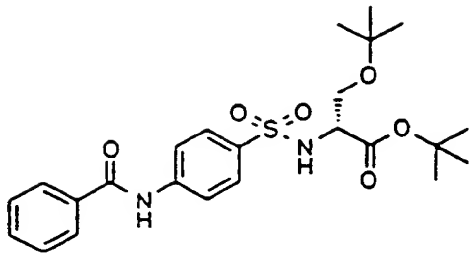
2-[N-[[4-(Benzoylamino)phenyl]sulfonyl]amino]-3-t-butoxy-L-propionic acid t-butyl ester



TLC: Rf 0.44 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.09 (1H, br.s), 7.9-7.75 (6H, m), 7.65-7.45 (3H, m), 5.45 (1H, d, J=9.4Hz), 4.0-3.95 (1H, m), 3.69 (1H, dd, J=3.8 5Hz), 3.52 (1H, dd, J=3.2, 8.5Hz), 1.32 (9H, s), 1.11 (9H, s).

Example 1(60)

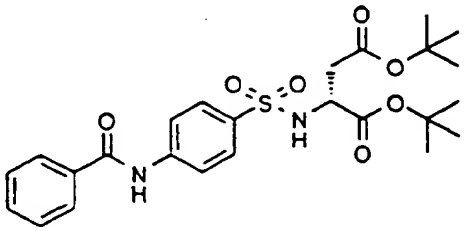
2-[N-[[4-(Benzoylamino)phenyl]sulfonyl]amino]-3-t-butoxy-D-propionic acid t-butyl ester



TLC: Rf 0.44 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.04 (1H, br.s), 7.9-7.75 (6H, m), 7.65-7.45 (3H, m), 5.44 (1H, d, J=9.2Hz), 4.0-3.95 (1H, m), 3.69 (1H, dd, J=3.0, 8.6Hz), 3.52 (1H, dd, J=3.2, 8.6Hz), 1.32 (9H, s), 1.11 (9H, s).

Example 1(61)

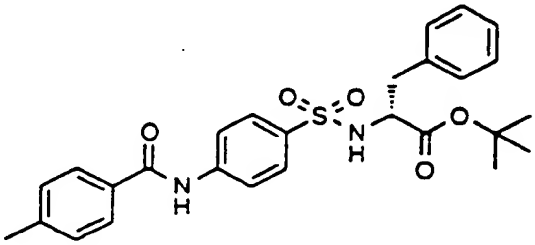
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-aspartic acid di-t-butyl ester



TLC: Rf 0.40 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.17 (1H, s), 7.9-7.75 (6H, m), 7.6-7.45 (3H, m), 5.64 (1H, d, J=8.0Hz), 3.99 (1H, m), 2.81 (1H, dd, J=4.6, 16.8Hz), 2.72 (1H, dd, J=4.6, 16.8Hz), 1.43 (9H, s), 1.33 (9H, s).

Example 1(62)

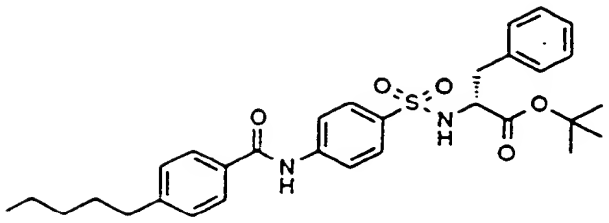
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-phenylalanine t-butyl ester



TLC: Rf 0.43 (Hexane : Ethyl acetate = 1 : 1),
NMR (CD_3OD + $CDCl_3$ (1:1)): δ 7.9-7.8 (4H, m), 7.71 (2H, d, J=8.8Hz), 7.35-7.1 (7H, m), 4.04 (1H, t, J=6.6Hz), 2.98 (2H, d, J=6.6Hz), 2.44 (3H, s), 1.23 (9H, s).

Example 1(63)

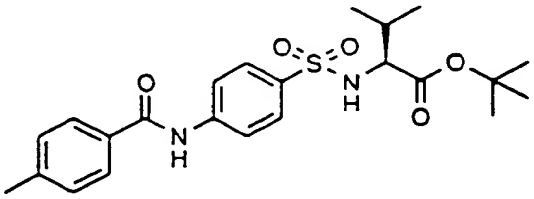
N-[[4-(4-Pentylbenzoylamino)phenyl]sulfonyl]-D-phenylalanine t-butyl ester



TLC. Rf 0.66 (Hexane . Ethyl acetate = 3 . 2).
NMR ($CDCl_3$): δ 7.95 (1H. s), 7.84-7.68 (6H. m), 7.35-7 08 (7H. m), 5.10 (1H. d. J=10.0Hz), 4.14-4.00 (1H. m), 3.02 (2H. d. J=6.0Hz), 2.67 (2H. t. J=7.8Hz), 1.72-1.56 (2H. m), 1.48-1.25 (4H. m), 1.21 (9H. s), 0.89 (3H. t.J=5.0Hz).

Example 1(64)

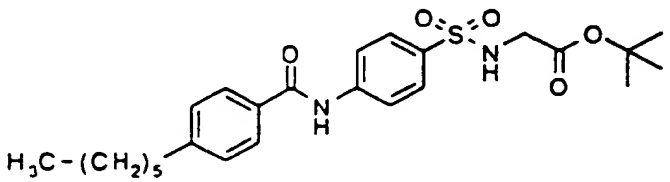
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-L-valine t-butyl ester



TLC: Rf 0.54 (Hexane : Ethyl acetate = 3 : 2).
NMR ($CDCl_3$): δ 7.93 (1H. s), 7.83 (2H. d. J=9.0Hz), 7.77 (2H. d. J=9.0Hz), 7.76 (2H. d. J=8.0Hz), 7.30 (2H. d. J=8.0Hz), 5.08 (1H. d. J=10.8Hz). 3.62 (1H. dd. J=4.4. 10.8Hz). 2.44 (3H. s). 2.15-1.90 (1H. m), 1.25 (9H. s), 1.00 (3H. d. J=6.6Hz), 0.85 (3H. d. J=6.6Hz).

Example 1(65)

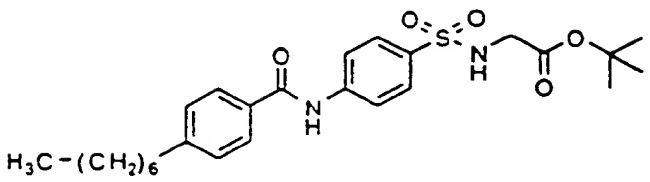
N-[[4-(4-Hexylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.26 (Hexane : Ethyl acetate = 7 : 3).
NMR ($CDCl_3$): δ 8.04 (1H. s). 7.85 (2H. d. J=9.0Hz). 7.79 (4H. m). 7.30 (2H. d. J=8.0Hz). 5.04 (1H. t. J=5.2Hz). 3.67 (2H. d. J=5.2Hz). 2.68 (2H. t. J=8.0Hz), 1.76-1.50 (2H. m), 1.37 (9H. s), 1.35-1.20 (6H. m), 0.88 (3H. t. J=6.8Hz).

Example 1(66)

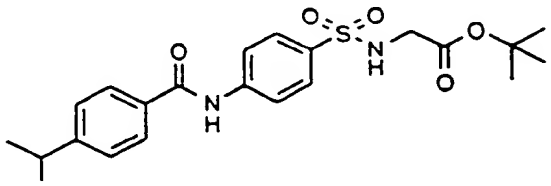
N-[[4-(4-Heptylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.29 (Hexane : Ethyl acetate = 7 : 3).
NMR ($CDCl_3$) δ 8.03 (1H, s), 7.85 (2H, d, J=9.0Hz), 7.79 (4H, m), 7.31 (2H, d, J=8.2Hz), 5.03 (1H, t, J=5.6Hz), 3.67 (2H, d, J=5.6Hz), 2.66 (2H, t, J=8.2Hz), 1.72-1.50 (2H, m), 1.37 (9H, s), 1.35-1.10 (8H, m), 0.88 (3H, t, J=6.8Hz).

Example 1(67)

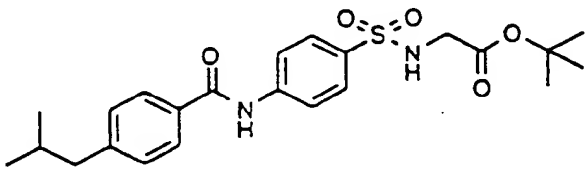
N-[[4-(4-Isopropylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.19 (Hexane : Ethyl acetate = 7 : 3).
NMR ($CDCl_3$): δ 8.01 (1H, s), 7.86 (2H, d, J=9.0Hz), 7.82-7.72 (4H, m), 7.36 (2H, d, J=8.4Hz), 5.01 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.99 (1H, m), 1.37 (9H, s), 1.29 (6H, d, J=6.8Hz).

Example 1(68)

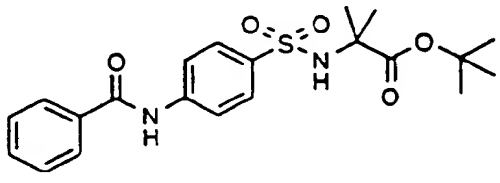
N-[[4-(4-Isobutylbenzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.23 (Hexane : Ethyl acetate = 7 : 3),
NMR ($CDCl_3$): δ 8.04 (1H, s), 7.86 (2H, d, J=9.0Hz), 7.82-7.72 (4H, m), 7.27 (2H, d, J=8.2Hz), 5.03 (1H, t, J=5.4Hz), 3.67 (2H, d, J=5.4Hz), 2.56 (2H, d, J=7.0Hz), 1.91 (1H, m), 1.37 (9H, s), 0.92 (6H, d, J=6.6Hz).

Example 1(69)

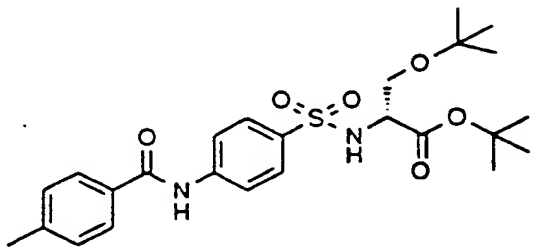
N-[[4-(Benzoylamino)phenyl]sulfonyl]-2,2-dimethylglycine t-butyl ester



TLC: Rf 0.40 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.03 (1H, s), 7.9-7.75 (6H, m), 7.65-7.45 (3H, m), 5.42 (1H, s), 1.45 (9H, s), 1.41 (6H, s).

Example 1(70)

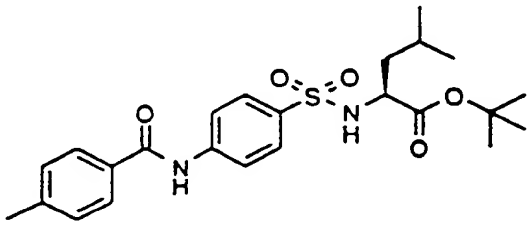
2-[N-[[4-(p-Toluoylamino)phenyl]sulfonyl]amino]-3-t-butoxy-D-propionic acid t-butyl ester



TLC: Rf 0.69 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 7.99 (1H, s), 7.85 (2H, d, J=8.0Hz), 7.78 (4H, d, J=8.0Hz), 7.30 (2H, d, J=8.0Hz), 5.43 (1H, d, J=9.2Hz), 3.97 (1H, td, J=3.0Hz, 9.2Hz), 3.69 (1H, dd, J=3.0Hz, 8.6Hz), 3.51 (1H, dd, J=3.0Hz, 8.6Hz), 2.43 (3H, s), 1.31 (9H, s), 1.10 (9H, s).

Example 1(71)

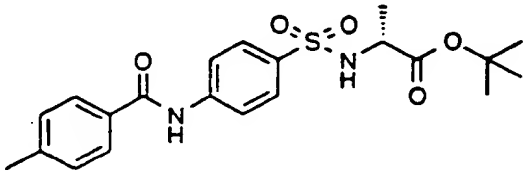
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-L-leucine t-butyl ester



TLC: Rf 0.50 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 7.90 (1H, s), 7.85-7.70 (6H, m), 7.32 (2H, d, J=8.0Hz), 5.02 (1H, d, J=10Hz), 3.90-3.75 (1H, m), 2.45 (3H, s), 1.9-1.75 (1H, m), 1.46 (2H, m), 1.26 (9H, s), 0.93 (6H, d, J=6.6Hz).

Example 1(72)

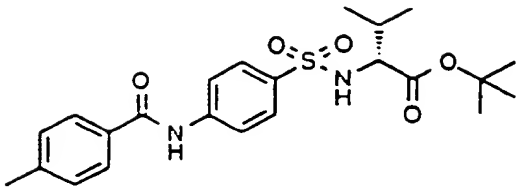
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-alanine t-butyl ester



TLC: Rf 0.57 (Hexane : Ethyl acetate = 1 : 1),
NMR (DMSO-d6): δ 10.47 (1H, s), 8.08 (1H, d, J=8.6Hz), 7.96 (2H, d, J=8.8Hz), 7.88 (2H, d, J=8.8Hz), 7.74 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.2Hz), 3.80-3.64 (1H, m), 2.39 (3H, s), 1.28 (9H, s), 1.15 (3H, d, J=7.0Hz).

Example 1(73)

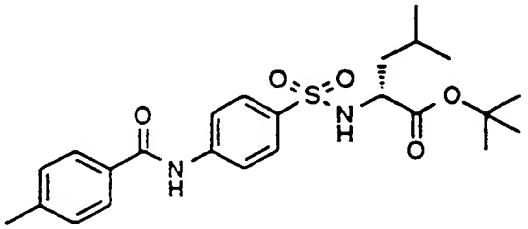
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-valine t-butyl ester



TLC: Rf 0.65 (Hexane : Ethyl acetate = 1 : 1).
NMR (DMSO-d6): δ 10.45 (1H, s), 8.02-7.92 (3H, m), 7.88 (2H, d, J=8.0Hz), 7.72 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.0Hz), 3.48-3.38 (1H, m), 2.39 (3H, s), 2.02-1.80 (1H, m), 1.22 (9H, s), 0.83 (6H, t, J=5.6Hz).

Example 1(74)

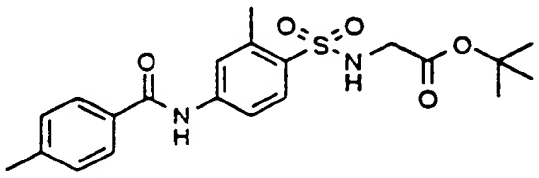
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-leucine t-butyl ester



TLC: Rf 0.68 (Hexane : Ethyl acetate = 1 : 1),
NMR (DMSO-d6): δ 10.45 (1H, s), 8.07 (1H, d, J=9.0H), 7.95 (2H, d, J=8.8Hz), 7.88 (2H, d, J=8.2Hz), 7.71 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.2Hz), 3.70-3.54 (1H, m), 2.39 (3H, s), 1.72-1.50 (1H, m), 1.44-1.30 (2H, m), 1.23 (9H, s), 0.84 (3H, d, J=6.6Hz), 0.76 (3H, d, J=6.6Hz).

Example 1(75)

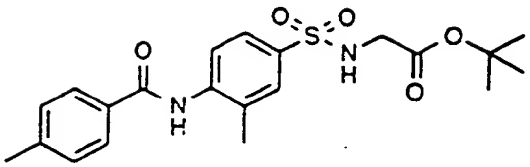
N-[[2-Methyl-4-(p-Toluoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.29 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 7.95 (2H, d, J=8.3Hz), 7.77 (2H, d, J=6.4Hz), 7.75-7.57 (2H, m), 7.31 (2H, d, J=8.3Hz), 5.10 (1H, m), 3.63 (2H, d, J=2.2Hz), 2.68 (3H, s), 2.44 (3H, s), 1.37 (9H, s).

Example 1(76)

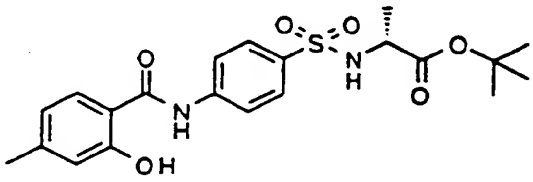
N-[[3-Methyl-4-(p-Toluoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.48 (Chloroform : Methanol = 97 : 3)
NMR ($CDCl_3$): δ 8.38 (1H, d, J=8.4Hz), 7.82-7.73 (4H, m), 7.33 (2H, d, J=7.8Hz), 5.00 (1H, t, J=4.7Hz), 3.67 (2H, d, J=4.7Hz), 2.45 (3H, s), 2.40 (3H, s), 1.38 (9H, s).

Example 1(77)

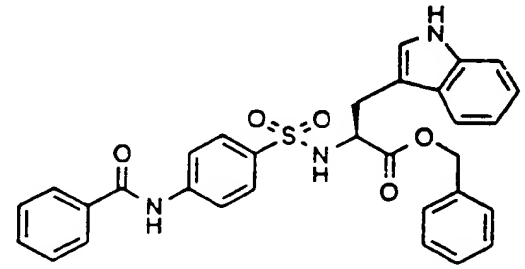
N-[[4-(2-Hydroxy-4-methylbenzoylamino)phenyl]sulfonyl]-D-alanine t-butyl ester



TLC: Rf 0.29 (Chloroform : Methanol = 97 : 3)
NMR ($CDCl_3$): δ 11.64 (1H, s), 8.09 (1H, br.s), 7.85 (2H, d, J=8.3Hz), 7.74 (2H, d, J=8.3Hz), 7.43 (1H, d, J=7.5Hz), 6.86 (1H, s), 6.75 (1H, d, J=7.5Hz), 5.25 (1H, t, J=7.6Hz), 3.87 (2H, quint, J=7.6Hz), 2.37 (3H, s), 1.37 (3H, d, J=7.6Hz), 1.32 (9H, s).

Example 1(78)

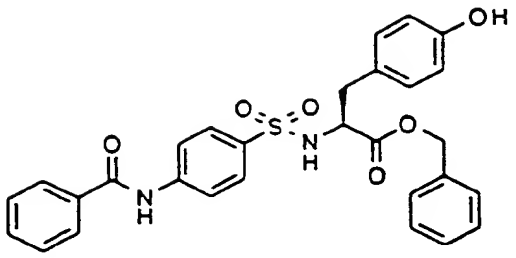
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-tryptophan benzyl ester



TLC: Rf 0.43 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 9.19 (1H, s), 7.94 (2H, dd, J=1.4, 7.8Hz), 7.68-7.40 (7H, m), 7.36-7.24 (5H, m), 7.18-6.98 (5H, m), 6.84 (1H, s), 4.91 (2H, s), 4.25 (1H, dd, J=5.2, 6.8Hz), 3.30-3.06 (2H, m).

Example 1(79)

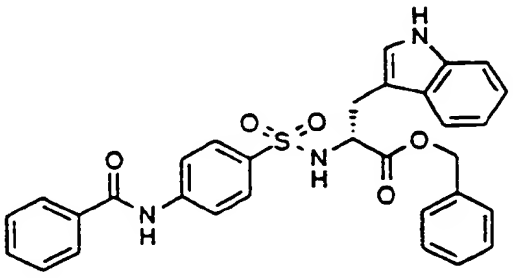
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-tyrosine benzyl ester



TLC: Rf 0.34 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$ + CD_3OD(10 drops)): δ 8.58 (1H, s), 7.80-7.78 (2H, m), 7.71 (2H, d, J=8.8Hz), 7.65-7.29 (8H, m), 7.25-7.17 (2H, m), 6.81 (2H, d, J=8.6Hz), 6.62 (2H, d, J=8.6Hz), 4.97 (2H, s), 4.10 (1H, dd, J=5.8, 7.8Hz), 2.99 (1H, dd, J=5.8, 14.0Hz), 2.81 (1H, dd, J=7.8, 14.0Hz).

Example 1(80)

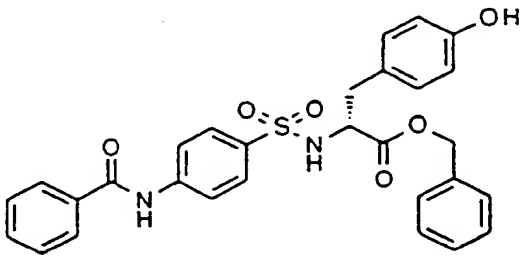
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-tryptophan benzyl ester



TLC: Rf 0.34 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$ + CD_3OD): δ 7.98-7.90 (2H, m), 7.63 (2H, d, J=8.8Hz), 7.60-7.39 (6H, m), 7.35-7.25 (5H, m), 7.17-6.97 (3H, m), 6.85 (1H, s), 4.91 (2H, s), 4.25 (1H, t, J=6.4Hz), 3.30-3.06 (2H, m).

Example 1(81)

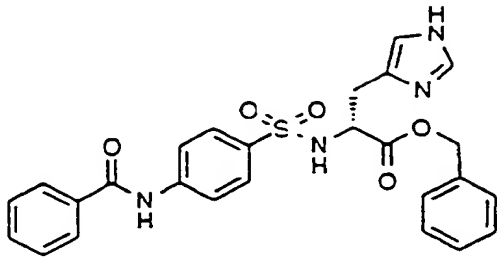
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-tyrosine benzyl ester



TLC: Rf 0.31 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.64-8.57 (1H, m), 8.15 (1H, s), 7.91 (2H, d, J=8.0Hz), 7.80-7.42 (6H, m), 7.40-7.20 (6H, m), 6.76 (2H, d, J=8.4Hz), 6.58 (2H, d, J=8.4Hz), 5.17 (1H, d, J=9.2Hz), 5.04 (2H, s), 4.18-4.04 (1H, m), 3.01 (1H, dd, J=5.0, 14.2Hz), 2.75 (1H, dd, J=7.8, 14.2Hz).

Example 1(82)

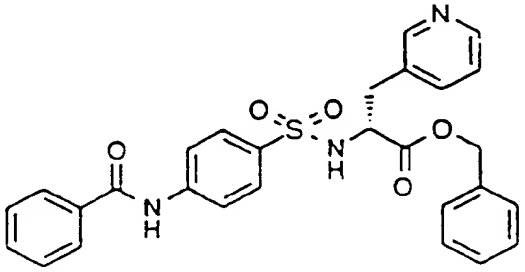
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-histidine benzyl ester



TLC: Rf 0.31 (Chloroform : Methanol = 9 : 1),
NMR ($CDCl_3$ + CD_3OD):δ 8.17 (1H, s), 7.96-7.80 (6H, m), 7.68-7.42 (3H, m), 7.40-7.22 (5H, m), 7.04 (1H, s), 5.10 (2H, s),3.80 (1H, dd, J=4.6Hz, 7.6Hz), 2.98 (1H, dd, J=4.6, 14.6Hz), 2.81 (1H, dd, J=7.6, 14.6Hz).

Example 1(83)

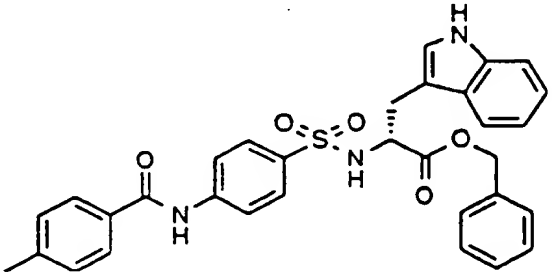
2-[N-[4-(Benzoylamino)phenyl]sulfonylamino]-(3-pyridyl)-D-alanine benzyl ester



TLC: Rf 0.32 (Hexane : Ethyl acetate = 1 : 5),
NMR ($CDCl_3$): δ 8.41 (1H, dd, J=2.0Hz, 5.0Hz), 8.25 (1H, d, J=2.0Hz), 8.08 (1H, s), 7.81 (2H, m), 7.74 (4H, s), 7.65-7.45 (3H, m), 7.35-7.3 (4H, m), 7.25-7.15 (2H, m), 7.09 (1H, dd, J=5, 8.0Hz), 5.58 (1H, d, J=8.0Hz), 4.97 (1H, s), 4.27 (1H, dt, J=6.0Hz, 8.0Hz), 3.05 (2H, d, J=6.0Hz).

Example 1(84)

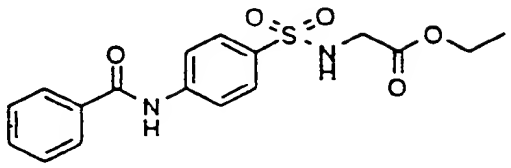
N-[[4-(p-Toluylamino)phenyl]sulfonyl]-D-tryptophan benzyl ester



TLC: Rf 0.32 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$ + CD_3OD):δ 7.81 (2H, d, J=8.0Hz), 7.56 (4H, s), 7.43 (1H, d, J=7.0Hz), 7.35-7.25 (6H, m), 7.15-7.00 (4H, m), 6.81 (1H, s), 4.92 (2H, s), 4.25 (1H, m), 3.18 (2H, m), 2.45 (3H,s).

Example 1(85)

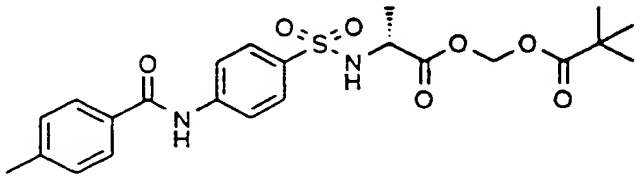
N-[[4-(Benzoylamino)phenyl]sulfonyl]glycine ethyl ester



TLC: Rf 0.26 (Hexane : Ethyl acetate = 1 : 1).
NMR (DMSO-d6): δ 10.59 (1H, s), 8.09 (1H, t, J=6.2Hz), 8.0-7.95 (4H, m), 7.77 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 4.00 (2H, q, J=7.0Hz), 3.68 (2H, d, J=6.2Hz), 1.12 (3H, t, J=7.0Hz).

Example 1(86)

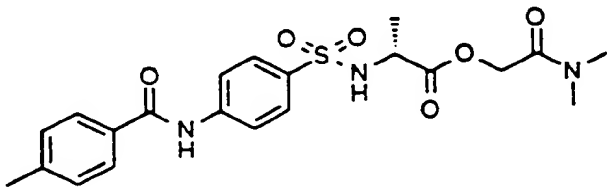
N-[[4-(p-Toluylamino)phenyl]sulfonyl]-D-alanine pivaloyloxymethyl ester



TLC: Rf 0.38 (Hexane : Ethyl acetate = 1 : 1).
NMR ($CDCl_3$): δ 8.05 (1H, br.s), 7.82 (4H, s), 7.78 (2H, d, J=8.0Hz), 7.31 (2H, d, J=8.0Hz), 5.67 (1H, d, J=14.6Hz), 5.59 (1H, d, J=14.6Hz), 5.15 (1H, br.d, J=8.8Hz), 4.03 (1H, m), 2.44 (3H, s), 1.39 (3H, d, J=7.0Hz), 1.17 (9H, s).

Example 1(87)

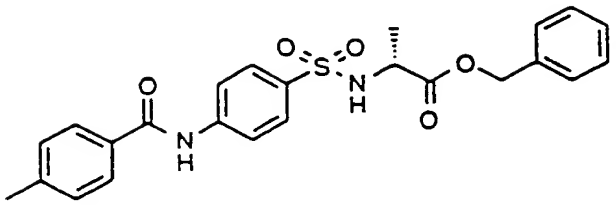
N-[[4-(p-Toluylamino)phenyl]sulfonyl]-D-alanine dimethyl aminocarbonyl ester



TLC: Rf 0.42 (Chloroform : Methanol : Acetic acid : Water = 100 :10 : 1 : 1),
NMR ($CDCl_3$ + CD_3OD (3 drops)): δ 7.82 (6H, m), 7.31 (2H, d, J=8.2Hz), 4.56 (1H, d, J=14.6Hz), 4.37 (1H, d, J=14.6Hz), 4.10 (1H, q, J=7.4Hz), 2.94 (3H, s), 2.90 (3H, s), 2.44 (3H, s), 1.46 (3H, d, J=7.4Hz).

Example 1(88)

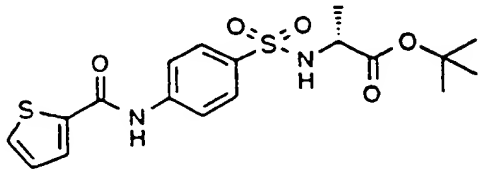
N-[[4-(p-Toluylamino)phenyl]sulfonyl]-D-alanine benzyl ester



TLC. Rf 0.56 (Chloroform . Methanol : Acetic acid : Water = 100 :10 : 1 : 1),
NMR (DMSO-d6): δ 10.49 (1H, s), 7.96 (3H. m), 7.69 (2H, d, J=8.0Hz), 7.74 (2H, d, J=8.8Hz), 7.4-7.25 (7H, m), 4.96 (2H, s), 3.94 (1H, m), 2.40 (3H, s), 1.19 (3H, d, J=7.2Hz).

Example 1(89)

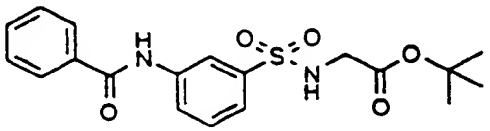
N-[[4-(2-Thienylcarbonylamino)phenyl]sulfonyl]-D-alanine t-butyl ester



TLC : Rf 0.25 (Hexane : Ethyl acetate = 2 : 1),
NMR (DMSO-d6): δ 10.51 (1H, s), 8.12-8.05 (2H, m), 7.94-7.88 (3H, m), 7.74 (2H, d, J=8.8Hz), 7.24 (1H, t, J=3.8Hz), 3.72 (1H. quint. J=7.4Hz), 1.27 (9H, s), 1.14 (3H. d, J=7.4Hz).

Example 1(90)

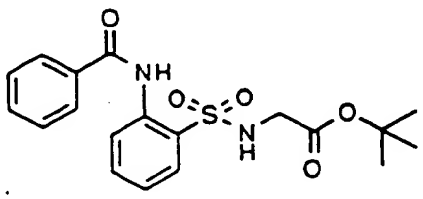
N-[[3-(Benzoylamino)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.65 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.26-8.16 (2H, m), 8.00 (1H. t, J=1.8Hz), 7.94-7.87 (2H, m), 7.66-7.46 (5H, m), 5.24 (1H, t, J=5.4Hz), 3.70 (2H. d. J=5.4Hz), 1.35 (9H. s).

Example 1(91)

N-[[2-(Benzoylamino)phenyl]sulfonyl]glycine t-butyl ester

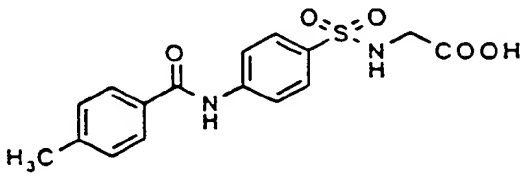


TLC: Rf 0.51 (Hexane : Ethyl acetate = 3 : 2).

NMR ($CDCl_3$): δ 10.27 (1H, s), 8.73 (1H, d, J=8.4 Hz), 8.05-7.94 (2H, m), 7.90 (1H, dd, J=1.8Hz, 8.0Hz), 7.70-7.45 (4H, m), 7.30-7.18 (1H, m), 5.20 (1H, t, J=5.2Hz), 3.61 (2H, d, J=5.2Hz), 1.33 (9H, s).

Example 2

N-[[4-(p-Toluoylamino)phenyl]sulfonyl]glycine

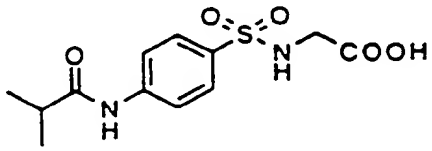


A mixture of the compound prepared in example 1 (1.45 g) in trifluoroacetic acid (10 ml) and water(1 ml) was stirred for 1 hour at room temperature. The reaction mixture was concentrated. The residue was washed with ether and dried to give the title compound (1.16 g) having the following physical data.
TLC: Rf 0.48 (Chloroform : Methanol : acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.46 (1H, s), 8.02-7.84 (1H), 7.97 (2H, d, J=9.0Hz), 7.88 (2H, d, J=8.0Hz), 7.75 (2H, d, J=9.0Hz), 7.34 (2H, d, J=8.0Hz), 3.55 (2H, d, J=6.2Hz), 2.40 (3H, s).

Example 2(1)-2(80)

The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 2, or converting to a corresponding salt by conventional method, using the compound prepared in Example 1(1)-1(77) and 1(89)-1(91) instead of the compound prepared in Example 1.

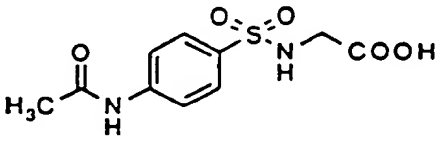
N-[[4-(Isobutyrylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.34 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (CD_3OD): δ 7.80 (2H, d, J=9.5Hz), 7.76 (2H, d, J=9.5Hz), 3.67 (2H, s), 2.64 (1H, m), 1.19 (6H, d, J=6.8Hz).

Example 2(2)

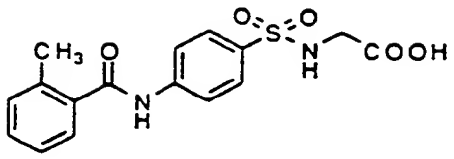
N-[[4-(Acetylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.23 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6):δ 10.26 (1H, s), 7.84 (1H, t, J=6.0Hz), 7.73 (2H, d, J=9.6Hz), 7.68 (2H, d, J=9.6Hz), 3.52 (2H, d, J=6.0Hz), 2.07 (3H, s).

Example 2(3)

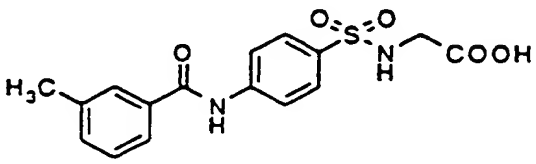
N-[[4-(o-Toluoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.48 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6).δ 10.63(1H, s), 7.91(2H, d, J=9.0Hz), 7.96-7.84 (1H), 7.74 (2H, d, J=9.0Hz), 7.51-7.24 (4H, m), 3.54 (2H, d, J=5.5Hz), 2.39 (3H, s).

Example 2(4)

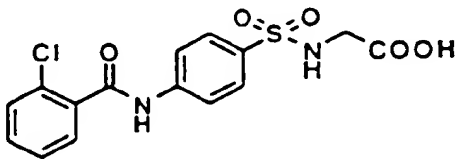
N-[[4-(3-Methylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.48 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6):δ 12.8-12.4 (1H, br.s), 10.49 (1H, s), 7.96(2H, d, J=8.8Hz), 7.88 (1H, t, J=6.2Hz), 7.75 (2H, d, J=8.8Hz), 7.80-7.70 (2H, m), 7.50-7.36 (2H, m), 3.55 (2H, d, J=6.2Hz), 2.41 (3H, s).

Example 2(5)

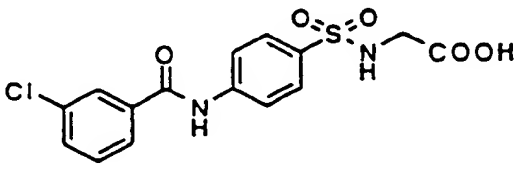
N-[[4-(2-Chlorobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.42 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (CD_3OD):δ 7.88 (2H, d, J=9.4Hz), 7.83 (2H, d, J=9.4Hz), 7.60-7.38 (4H, m), 3.70 (2H, s).

Example 2(6)

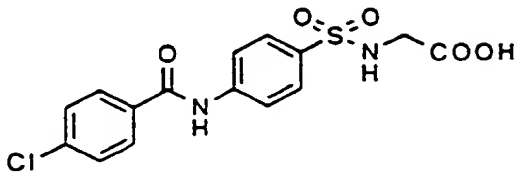
N-[[4-(3-Chlorobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.42 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (CD_3OD):δ 7.99-7.94 (1H, m), 7.93 (2H, d, J=9.0Hz), 7.93-7.80 (1H, m), 7.84 (2H, d, J=9.0Hz), 7.64-7.46 (2H, m), 3.69 (2H, s).

Example 2(7)

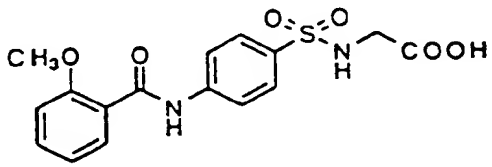
N-[[4-(4-Chlorobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.42 (Chloroform : Methanol : Acetic acid = 16 . 3 : 1),
NMR (CD_3OD): δ 7.94 (2H, d, J=8.6Hz), 7.92 (2H, d, J=9.0Hz), 7.84 (2H, d, J=9.0Hz), 7.53 (2H, d, J=8.6Hz), 3.70 (2H, s).

Example 2(8)

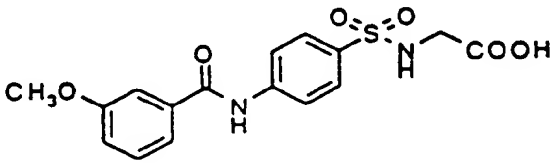
N-[[4-(2-Methoxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.58 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.45 (1H, s), 7.91 (1H, t, J=6.2Hz), 7.90 (2H, d, J=8.8Hz), 7.75 (2H, d, J=8.8Hz), 7.61 (1H, dd, J=7.4, 1.6Hz), 7.52 (1H, ddd, J=8.4, 7.4, 2.0Hz), 7.18 (1H, d, J=8.0Hz), 7.07 (1 H, td, J=7.6, 1.0Hz), 3.89 (3H, s), 3.56 (2H, d, J=6.2Hz).

Example 2(9)

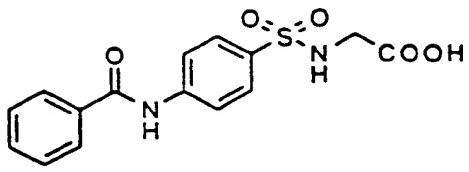
N-[[4-(3-Methoxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.44 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.52 (1H, s), 7.96 (2H, d, J=8.8Hz), 7.91 (1H, t, J=6.2Hz), 7.76 (2H, d, J=8.8Hz), 7.58-7.41 (3H, m), 7.21-7.14 (1H, m), 3.84 (3H, s), 3.56 (2H, d, J=6.2Hz).

Example 2(10)

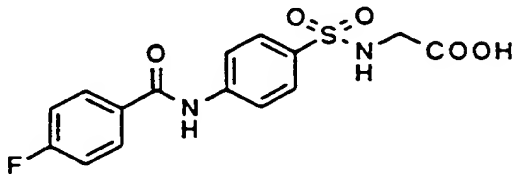
N-[[4-(Benzoylamino)phenyl]sulfonyl]glycine



TLC. Rf 0 19 (Chloroform : Methanol : Acetic acid : Water = 50 : 10 : 1 : 1),
NMR (CD_3OD): δ 6.0-7.8 (6H, m), 7.6-7.5 (3H, m), 3.70 (2H, s).

Example 2(11)

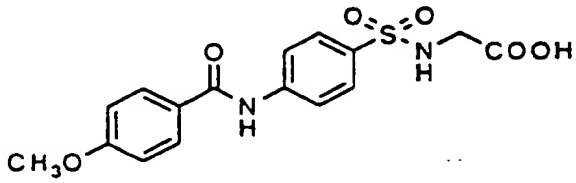
N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.36 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1).
NMR (DMSO-d6):δ 10.56 (1H, s), 8.05 (2H, dd, J=8.8, 5.4Hz), 7.96 (2H, d, J=9.2Hz), 7.91 (1H, t, J=6.2Hz), 7.77 (2H, d, J=9.2Hz), 3.56 (2H, d, J=6.2Hz).

Example 2(12)

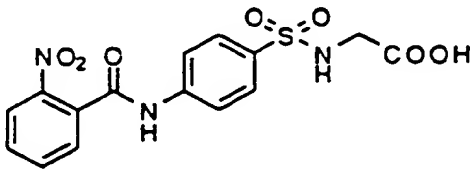
N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.43 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.39 (1H, s), 7.97 (2H, d, J=8.8Hz), 7.95 (2H, d, J=9.0Hz), 7.89 (1H, t, J=6.2Hz), 7.75 (2H, d, J=9.0Hz), 7.70 (2H, d, J=8.8Hz), 3.84 (3H, s), 3.55 (2H, d, J=6.2Hz).

Example 2(13)

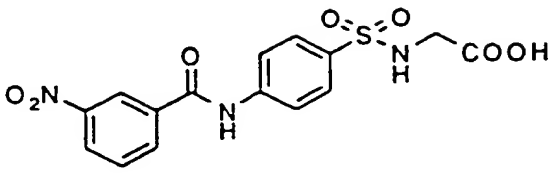
N-[[4-(2-Nitrobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.44 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.65 (1H, br.s), 11.02 (1H, s), 8.18 (1H, d, J=7.8Hz), 8.0-7.7 (8H, m), 3.57 (2H, d, J=6.0Hz).

Example 2(14)

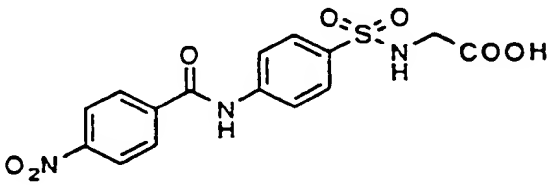
N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.56 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1).
NMR (DMSO-d6): δ 12.65 (1H, br.s), 10.89 (1H, s), 8.81 (1H, t, J=2.0Hz), 8.5-8.4 (2H, m), 8.0-7.85 (4H, m), 7.81 (2H, d, J=8.8Hz), 3.57 (2H, d, J=6.0Hz).

Example 2(15)

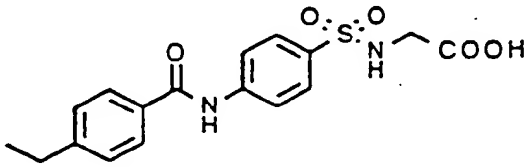
N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.55 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6):δ 12.65 (1H, br.s), 10.88 (1H, s), 8.39 (2H, d, J=9.0Hz), 8.20 (2H, d, J=9.0Hz), 7.98 (d, J=8.8Hz) and 7.96 (t, J=6.0Hz) (total 3H), 7.80 (2H, d, J=8.8Hz), 3.58 (2H, d, J=6.0Hz).

Example 2(16)

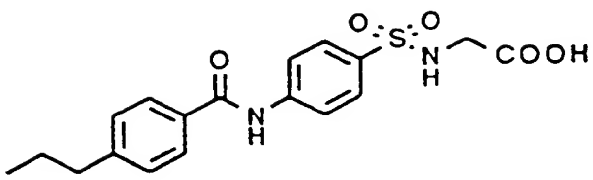
N-[[4-(4-Ethylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.53 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (CD_3OD): δ 7.93 (2H, d, J=9.0Hz), 7.87 (2H, d, J=8.6Hz), 7.83 (2H, d, J=9.0Hz), 7.36 (2H, d, J=8.6Hz), 3.69 (2H, s), 2.73 (2H, q, J=7.6Hz), 1.27 (3H, t, J=7.6Hz).

Example 2(17)

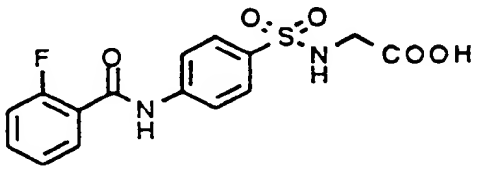
N-[[4-(4-Propylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.54 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (CD_3OD): δ 7.93 (2H, d, J=9.0Hz), 7.86 (2H, d, J=8.2Hz), 7.83 (2H, d, J=9.0Hz), 7.33 (2H, d, J=8.2Hz), 3.69 (2H, s), 2.68 (2H, dd, J=7.4, 8.2Hz), 1.80-1.60 (2H, m), 0.96 (3H, t, J=7.2Hz).

Example 2(18)

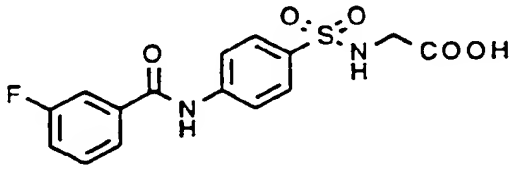
N-[[4-(2-Fluorobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.48 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.40-11.60 (1H, br.s), 10.74 (1H, s), 7.96-7.84 (1H, t, J=6.0Hz), 7.89 (2H, d, J=8.8Hz), 7.76 (2H, d, J=8.8Hz), 7.72-7.52 (2H, m), 7.42-7.28 (2H, m), 3.55 (2H, d, J=6.0Hz).

Example 2(19)

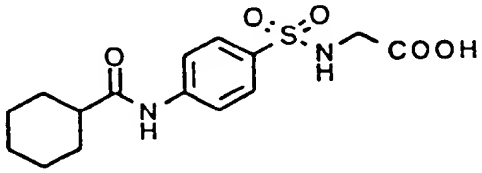
N-[[4-(3-Fluorobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.38 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.40-11.60 (1H, br.s), 10.61 (1H, s), 7.96 (2H, d, J=8.8Hz), 7.92 (1H, t, J=6.0Hz), 7.87-7.72 (2H, m), 7.77 (2H, d, J=8.8Hz), 7.67-7.40 (2H, m), 3.56 (2H, d, J=6.0Hz).

Example 2(20)

N-[[4-(Cyclohexylcarbonylamino)phenyl]sulfonyl]glycine

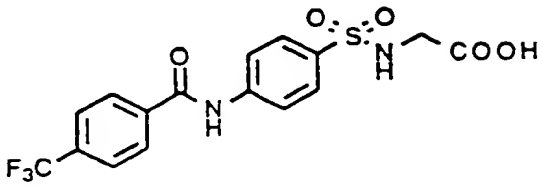


TLC: Rf 0.43 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR ($CDCl_3$ + CD_3OD(10 drops)): δ 7.77 (2H, d, J=8.8Hz), 7.68 (2H, d, J=8.8Hz), 3.71 (2H, s), 2.40-2.20 (1H, m),

2.00-1.20 (10H. m).

Example 2(21)

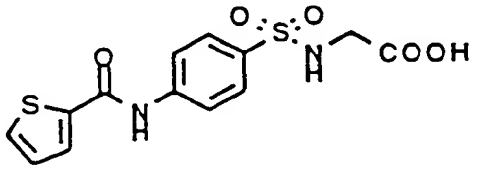
N-[[4-(4-Trifluoromethylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.40 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.40-11.60 (1H, br.s), 10.76 (1H, s), 8.16 (2H, d, J=8.0Hz), 8.03-7.87 (1H, t, J=6.2Hz), 7.97 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.0Hz), 7.78 (2H, d, J=8.8Hz), 3.57 (2H, d, J=6.2Hz).

Example 2(22)

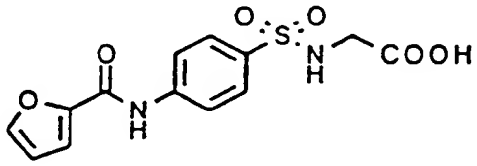
N-[[4-(2-Thienylcarbonylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.47 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.60 (1H, br.s), 10.52 (1H, s), 8.06 (1H, d, J=3.8Hz), 8.0-7.9 (4H, m), 7.77 (2H, d, J=8.8Hz), 7.25 (1H. dd. J=3.8. 5.0Hz). 3.57 (2H. d, J=5.8Hz).

Example 2(23)

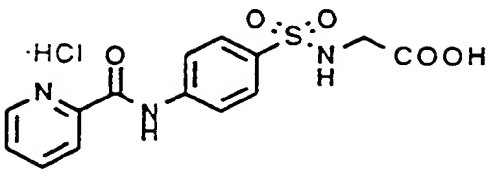
N-[[4-(2-Furylcarbonylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.45 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.65 (1H, br.s), 10.51 (1H, s), 8.0-7.9 (4H, m), 7.75 (2H, d, J=8.8Hz), 7.40 (1H, d, J=3.4Hz), 6.73 (1H, dd. J=1.6. 3.4Hz), 3.57 (2H, d, J=6.0Hz).

Example 2(24)

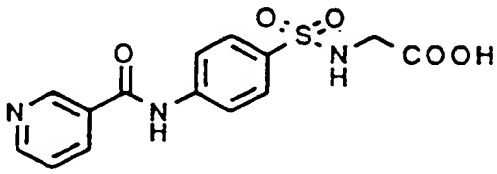
N-[[4-(2-Pyridylcarbonylamino)phenyl]sulfonyl]glycine hydrochloride



TLC: Rf 0.50 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.98 (1H, s), 8.76 (1H, d, J=4.6Hz), 8.24-8.02 (2H, m), 8.12 (2H, d, J=8.8Hz), 8.01-7.82 (1H, br. s), 7.77 (2H, d, J=8.8Hz), 7.74-7.65 (1H, m), 3.57 (2H, d, J=5.4Hz).

Example 2(25)

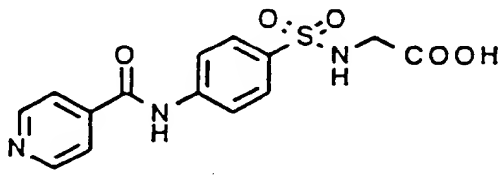
N-[[4-(3-Pyridylcarbonylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.25 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 10.76 (1H, s), 9.12 (1H, d, J=1.8Hz), 8.77 (1H, dd, J=1.8, 5.0Hz), 8.31 (1H, dt, J=1.8, 8.2Hz), 7.97 (2H, d, J=9.0Hz), 7.93 (1H, t, J=5.4Hz), 7.79 (2H, d, J=9.0Hz), 7.58 (1H, dd, J=5.0, 8.2Hz), 3.57 (2H, d, J=5.4Hz).

Example 2(26)

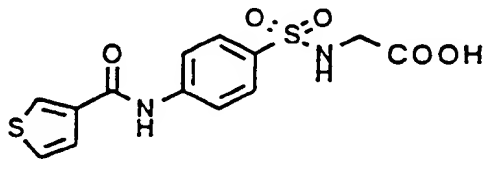
N-[[4-(4-Pyridylcarbonylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.20 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.20-12.00 (1H, br.s), 10.80 (1H, s), 8.83-8.76 (2H, m), 8.02-7.90 (1H, t, J=6.2Hz), 7.97 (2H, d, J=8.8Hz), 7.89-7.85 (2H, m), 7.79 (2H, d, J=8.8Hz), 3.57 (2H, d, J=6.2Hz).

Example 2(27)

N-[[4-(3-Thienylcarbonylamino)phenyl]sulfonyl]glycine

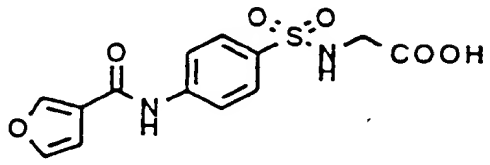


TLC: Rf 0.45 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),

NMR (DMSO-d6): δ 12.5 (1H, br.s), 10.36 (1H. s), 8.4 (1H. m), 7.95-7.9 (3H. m), 7.76 (2H. d, J=8.9Hz), 7.65 (2H. m), 3.57 (2H, d, J=6.0Hz).

Example 2(28)

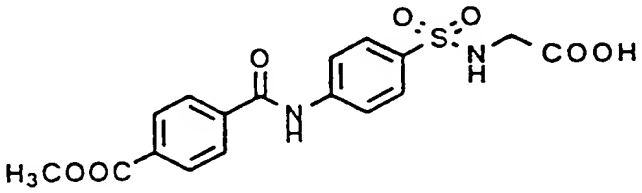
N-[[4-(3-Furylcarbonylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.67 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.6 (1H, br.s), 10.23 (1H, s), 8.43 (1H, m), 7.95-7.85 (3H, m), 7.82 (1H, m), 7.76 (2H, d, J=8.7Hz), 7.01 (1H, m), 3.57 (2H, d, J=6.0Hz).

Example 2(29)

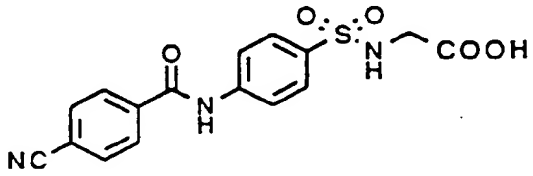
N-[[4-(4-Methoxycarbonylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.41 (Chloroform : Methanol Acetic acid = 16 : 3 : 1),
NMR(DMSO-d6): δ 13.50-11.50 (1H, br.s), 10.75 (1H, s), 8.12 (2H, d, J=9.2Hz), 8.07 (2H, d, J=9.2Hz), 7.98 (2H, d, J=8.8Hz), 7.94 (1 H, t, J=6.0Hz), 7.78 (2H, d. J=8.8Hz), 3.90 (3H, s), 3.58 (2H, d, J=6.0Hz).

Example 2(30)

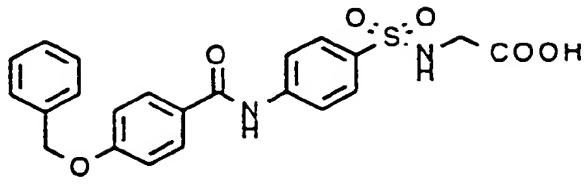
N-[[4-(4-Cyanobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.34 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H. br.s), 10.79 (1H. s), 8.12 (2H, d, J=8.8Hz), 8.04 (2H, d, J=8.8Hz), 8.01-7.90 (1H), 7.96 (2H. d, J=8.8Hz), 7.79 (2H, d, J=8.8Hz). 3.58 (2H, d, J=6.2Hz).

Example 2(31)

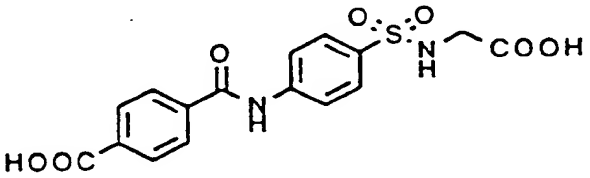
N-[[4-(4-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.48 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 10.41 (1H, s), 7.97 (2H, d, J=8.8Hz), 7.96 (2H, d, J=8.8Hz), 7.90 (1H, t, J=6.2Hz), 7.75 (2H, d, J=8.8Hz), 7.54-7.28 (5H, m), 7.16 (2H, d, J=8.8Hz), 5.21 (2H, s), 3.57 (2H, d, J=6.2Hz).

Example 2(32)

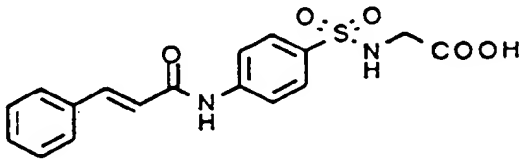
N-[[4-(4-Carboxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.51 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 13.3-12.70 (1H, br.s), 10.74 (1H, s), 8.11 (2H, d, J=9.0Hz), 8.06 (2H, d, J=9.0Hz), 7.98 (2H, d, J=8.8Hz), 7.94 (1H, t, J=6.2Hz), 7.79 (2H, d, J=8.8Hz), 3.58 (2H, d, J=6.2Hz).

Example 2(33)

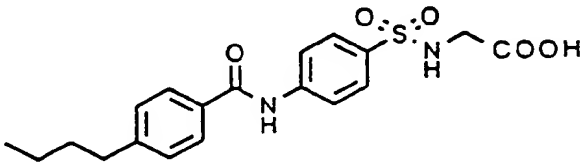
N-[[4-(Cinnamoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.45 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 12.80-12.40 (1H, br.s), 10.57 (1H, s), 7.91 (1H, t, J=6.2Hz), 7.87 (2H, d, J=8.8Hz), 7.75 (2H, d, J=8.8Hz), 7.70-7.52 (3H, m), 7.50-7.38 (3H, m), 6.85 (1H, d, J=15.8Hz), 3.56 (2H, d, J=6.2Hz).

Example 2(34)

N-[[4-[(4-Butylbenzoylamino)phenyl]sulfonyl]glycine

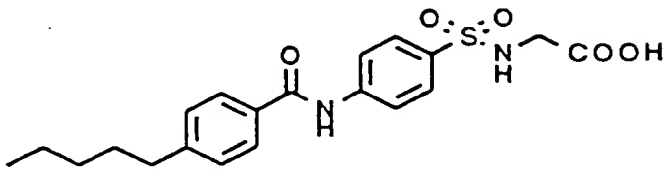


TLC: Rf 0.55 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.40-11.60 (1H, br.s), 10.47 (1H, s), 7.80 (1H, br.t, J=6.0Hz), 7.96 (2H, d, J=8.8Hz), 7.88 (2H, d,

J=8.2Hz), 7.75 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.2Hz), 3.56 (2H, d, J=6.0Hz), 2.64 (2H, t, J=7.6Hz), 1.76-1.42 (2H, m), 1.42-1.10 (2H, m), 0.90 (3H, t, J=7.4Hz).

Example 2(35)

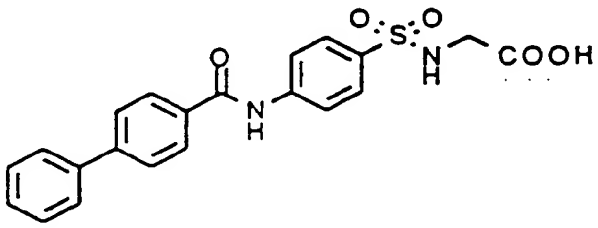
N-[[4-(4-Pentylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.55 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.40-11.60 (1H, br.s), 10.48 (1H, s), 7.90 (1H, br.t, J=6.0Hz), 7.97 (2H, d, J=8.8Hz), 7.89 (2H, d, J=8.2Hz), 7.76 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.2Hz), 3.56 (2H, d, J=6.0Hz), 2.66 (2H, t, J=7.0Hz), 1.72-1.48 (2H, m), 1.48-1.18 (4H, m), 0.87 (3H, t, J=6.6Hz).

Example 2(36)

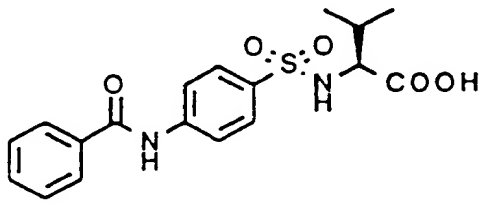
N-[[4-(4-Phenylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.50 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.40-11.60 (1H, br.s), 10.62 (1H, s), 8.08 (2H, d, J=8.4Hz), 8.01 (2H, d, J=8.8Hz), 7.93 (1H, t, J=6.0Hz), 7.90-7.70 (2H, m), 7.85 (2H, d, J=8.4Hz), 7.77 (2H, d, J=8.8Hz), 7.60-7.36 (3H, m), 3.58 (2H, d, J=6.0Hz).

Example 2(37)

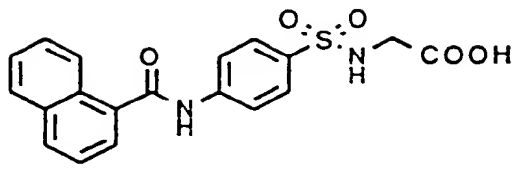
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-valine



TLC: Rf 0.75 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.6 (1H, br.s), 10.57 (1H, s), 8.0-7.9 (5H, m), 7.75 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 3.51 (1H, dd, J=6, 9.4Hz), 2.0-1.85 (1H, m), 0.83 (3H, d, J=6.8Hz), 0.81 (3H, d, J=6.8Hz).

Example 2(38)

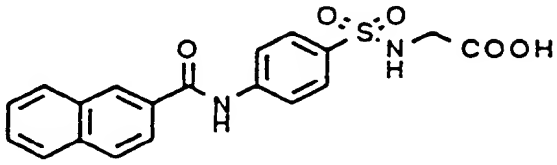
N-[[4-(1-Naphthoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.49 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 10.92 (1H. s), 8.26-7.86 (6H, m), 7.85-7.70 (3H, m), 7.68-7.50 (3H. m), 3.58 (2H, d, J=5.8Hz).

Example 2(39)

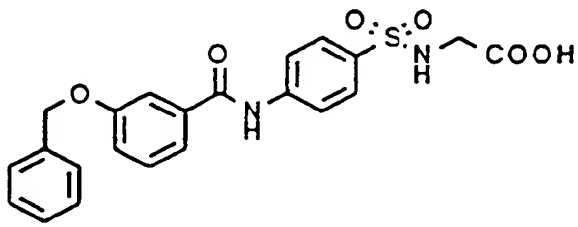
N-[[4-(2-Naphthoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.49 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 10.75 (1H, s), 8.61 (1H, s), 8.15-7.99 (6H, m), 7.94 (1H, t, J=6.2Hz), 7.81 (2H. d. J=9.2Hz), 7.72-7.58 (2H, m), 3.59 (2H, d, J=6.2Hz).

Example 2(40)

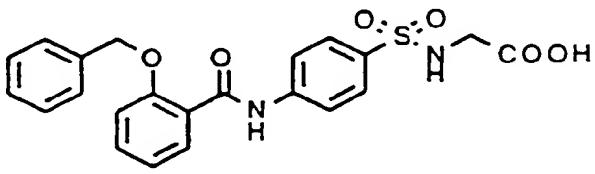
N-[[4-(3-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.54 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H. br.s), 10.51 (1H, s), 7.96 (2H, d, J=8.8Hz), 7.90 (1 H, t, J=6.2Hz), 7.76 (2H, d, J=8.8Hz), 7.62-7.22 (9H, m), 5.19 (2H, s), 3.56 (2H, d, J=6.2Hz).

Example 2(41)

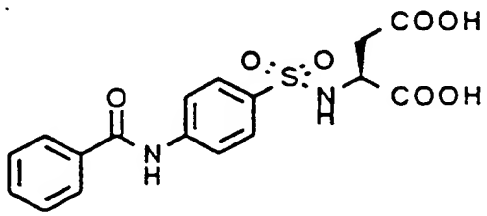
N-[[4-(2-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.73 (Chloroform : Methanol : Acetic acid =16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 10.50 (1H, s), 7.89 (1H, t, J=6.2Hz), 7.78-7.67 (4H, m), 7.68 (1H, dd, J=1.6, 7.6Hz), 7.60-7.48 (3H, m), 7.44-7.25 (4H, m), 7.10 (1H, dt, J=0.8, 7.6Hz), 5.24 (2H, s), 3.54 (2H, d, J=6.2Hz).

Example 2(42)

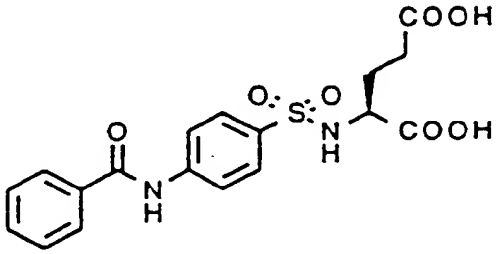
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-aspartic acid



TLC: Rf 0.35 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (CD_3OD): δ 8.00-7.80 (6H, m), 7.65-7.50 (3H, m), 4.22 (1H, t, J=9.0Hz), 2.73 (2H, d, J=6.0Hz).

Example 2(43)

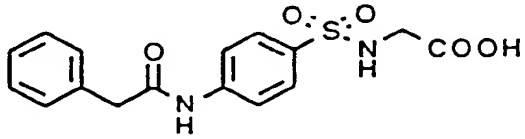
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-glutamic acid



TLC: Rf 0.49 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (CD_3OD): δ 8.00-7.80 (6H, m), 7.65-7.50 (3H, m), 3.93 (1H, dd, J=2.8, 9.0Hz), 2.41 (2H, t, J=7.5Hz), 2.15-1.95 (1H, m), 1.90-1.75 (1H, m).

Example 2(44)

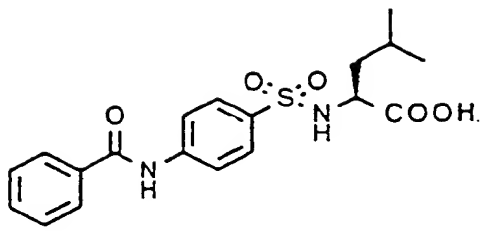
N-[[4-(Phenylacetylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.44 (Chloroform : Methanol : Acetic acid =16 : 3 : 1),
NMR (DMSO-d6): δ 10.51 (1H, s), 7.86 (1H, t, J=6.2Hz), 7.76 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.8Hz), 7.40-7.18 (5H, m), 3.67 (2H, s), 3.53 (2H, d, J=6.2Hz).

Example 2(45)

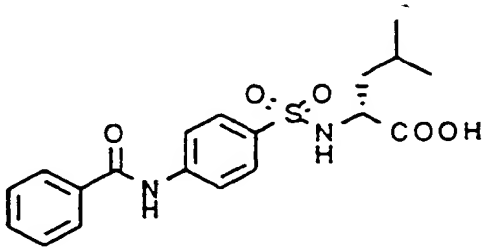
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-leucine



TLC: Rf 0.41 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 10.29 (1H, s), 8.16 (1H, br.t, J=9.0Hz), 7.97 (2H, m), 7.72 (2H, d, J=8.6Hz), 7.6-7.45 (5H, m), 3.86 (1H, m), 1.8-1.5 (3H, m), 0.91 (6H, d, J=5.4Hz).

Example 2(46)

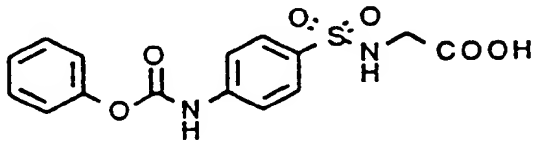
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-leucine



TLC: Rf 0.41 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 10.29 (1H, s), 8.16 (1H, br.t, J=9.0Hz), 7.97 (2H, m), 7.72 (2H, d, J=8.8Hz), 7.6-7.45 (5H, m), 3.86 (1H, m), 1.8-1.5 (3H, m), 0.90 (6H, d, J=6.2Hz).

Example 2(47)

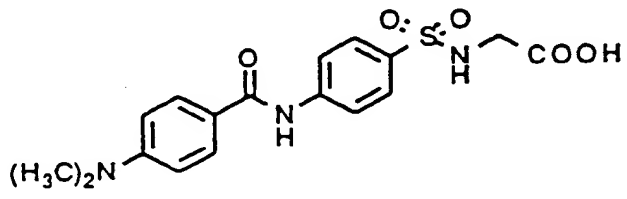
N-[[4-(Phenoxycarbonylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.44 (Chloroform : Methanol : Acetic acid =16 : 3 : 1),
NMR (DMSO-d6): δ 13.20-12.00 (1H, br.s), 10.64 (1H, s), 7.89 (1H, t, J=6.2Hz), 7.75 (2H, d, J=8.8Hz), 7.65 (2H, d, J=8.8Hz), 7.51-7.38 (2H, m), 7.33-7.20 (3H, m), 3.55 (2H, d, J=6.2Hz).

Example 2(48)

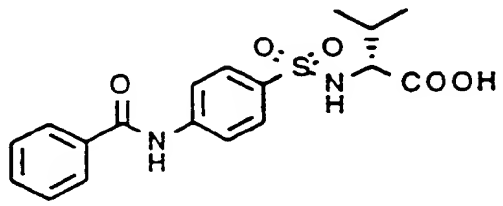
N-[[4-(4-Dimethylaminobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.54 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 10.18 (1H, s), 8.00-7.80 (5H, m), 7.73 (2H, d, J=8.8Hz), 6.77 (2H, d, J=9.0Hz), 3.55 (2H), 3.03 (6H, s).

Example 2(49)

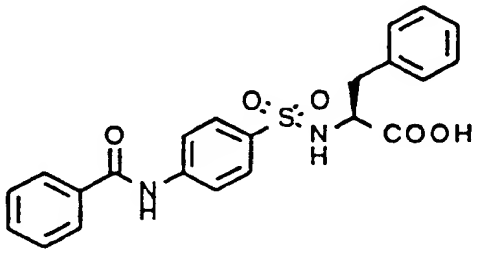
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-valine



TLC: Rf 0.73 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.6 (1H, br.s), 10.56 (1H, s), 8.0-7.85 (5H, m), 7.75 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 3.51 (1H, dd, J=6.1, 9.3Hz), 2.0-1.85 (1H, m), 0.83 (3H, d, J=6.8Hz), 0.81 (3H, d, J=6.8Hz).

Example 2(50)

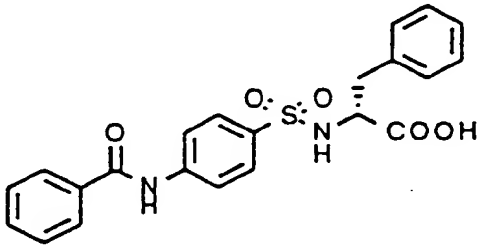
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-Phenylalanine



TLC: Rf 0.68 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.71 (1H, br.s), 10.54 (1H, s), 8.17 (1H, d, J=9.0Hz), 7.97 (2H, m), 7.86 (2H, m), 7.65-7.5 (5H, m), 7.25-7.1 (5H, m), 3.95-3.8 (1H, m), 2.94 (1H, dd, J=5.8, 13.8Hz), 2.72 (1H, dd, J=8.8, 13.8Hz).

Example 2(51)

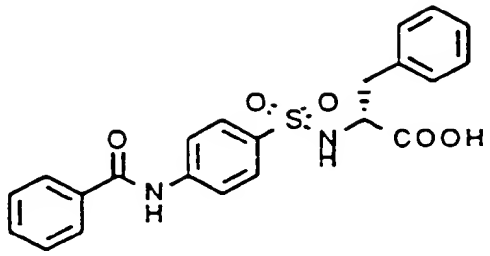
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-Phenylalanine



TLC: Rf 0.68 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.71 (1H, br.s), 10.53 (1H, s), 8.17 (1H, d, J=9.0Hz), 7.97 (2H, m), 7.86 (2H, m), 7.65-7.5 (5H, m), 7.3-7.1 (5H, m), 3.95-3.8 (1H, m), 2.94 (1H, dd, J=5.8, 13.8Hz), 2.73 (1H, dd, J=8.4, 13.8Hz).

Example 2(52)

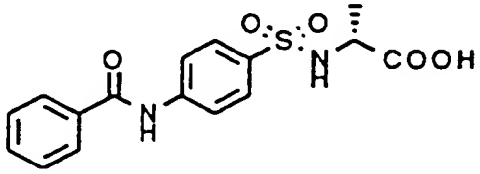
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-alanine



TLC: Rf 0.62 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR(DMSO-d6): δ 12.6 (1H, br.s), 10.58 (1H, s), 8.04 (1H, d, J=8.6Hz), 8.0-7.9 (4H, m), 7.76 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 3.75 (1H, m), 1.16 (3H, d, J=7.4Hz).

Example 2(53)

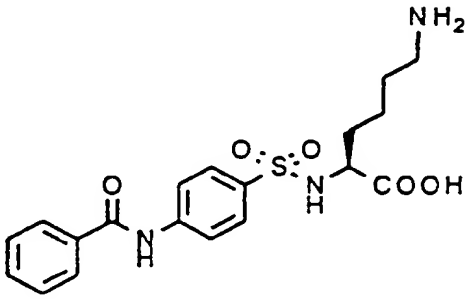
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-alanine



TLC: Rf 0.62 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.6 (1H, br.s), 10.58 (1H, s), 8.04 (1H, d, J=8.6Hz), 8.0-7.9 (4H, m), 7.77 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 3.76 (1H, m), 1.16 (3H, d, J=7.4Hz).

Example 2(54)

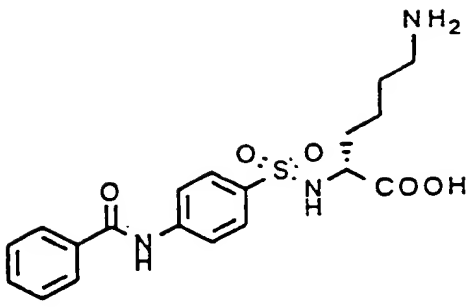
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-lysine



TLC: Rf 0.19 (Chloroform : Methanol : Acetic acid : Water = 2 : 1 : 0.1 : tailing),
NMR (DMSO-d6 + CF_3COOH(1 drop)): δ 10.59 (1H, s), 8.05-7.95 (5H, m), 7.80-7.50 (4H, m), 3.70-3.60 (1H, m), 2.80-2.65 (2H, m), 1.70-1.20 (6H, m).

Example 2(55)

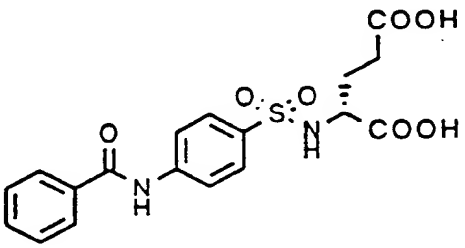
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-lysine



TLC: Rf 0.19 (Chloroform : Methanol : Acetic acid : Water = 2 : 1 : 0.1 : tailing),
NMR (DMSO-d6 + CF_3COOH(1 drop)): δ 10.59 (1H, s), 8.05-7.95 (5H, m), 7.80-7.50 (4H, m), 3.70-3.60 (1H, m), 2.80-2.65 (2H, m), 1.70-1.20 (6H, m).

Example 2(56)

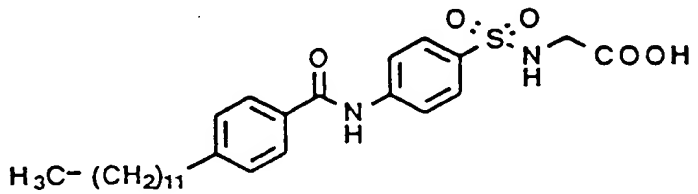
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-glutamic acid



TLC: Rf 0.45 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.4 (2H, br.s), 10.57 (1H, s), 8.05 (1H, d, J=9.0Hz), 7.97 (4H, m), 7.74 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 3.76 (1H, m), 2.23 (2H, t, J=7.4Hz), 1.95-1.55 (2H, m).

Example 2(57)

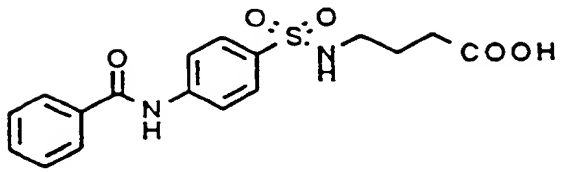
N-[[4-(4-Dodecylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.68 (Chloroform : Methanol : Acetic acid =16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 10.46 (1H, s), 7.97 (2H, d, J=8.8Hz), 7.89 (1H, t, J=6.2Hz), 7.88 (2H, d, J=8.4Hz), 7.76 (2H, d, J=8.8Hz), 7.34 (2H, d, J=8.4Hz), 3.55 (2H, d, J=6.2Hz), 2.65 (2H, t, J=7.8Hz), 1.70-1.48 (2H, m), 1.40-1.10 (18H, m), 0.85 (3H, t, J=6.6Hz).

Example 2(58)

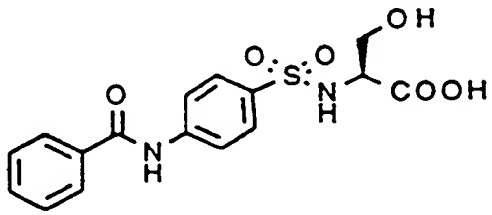
4-[N-[[4-(Benzoylamino)phenyl]sulfonyl]amino]butyric acid



TLC: Rf 0.76 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.05 (1H, br.s), 10.59 (1H, s), 8.05-7.95 (4H, m), 7.76 (2H, d, J=8.8Hz), 7.65-7.45 (4H, m), 2.75 (2H, q, J=6.8Hz), 2 .22 (2H, d, J=7.2Hz), 1.60 (2H, m).

Example 2(59)

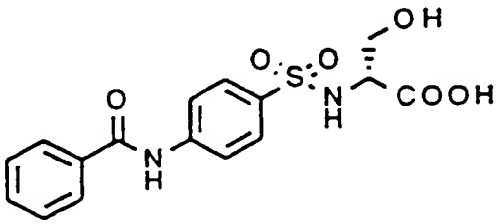
N-[[4-(Benzoylamino)phenyl]sulfonyl]amino]-L-serine



TLC: Rf 0.42 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 10.57 (1H, s), 8.0-7.95 (4H, m), 7.88 (1H, d, J=8.6Hz), 7.76 (2H, d, J=8.6Hz), 7.65-7.5 (3H, m), 3.74 (1H. m), 3.49 (2H. d. J=5.2Hz).

Example 2(60)

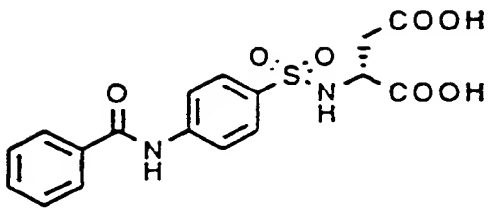
N-[[4-(Benzoylamino)phenyl]sulfonyl]amino]-D-serine



TLC: Rf 0.42 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 10.57 (1H, s), 8.0-7.9 (4H, m), 7.88 (1H, d, J=8.6Hz), 7.76 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 3.75 (1H. m), 3.49 (2H, d, J=5.4Hz).

Example 2(61)

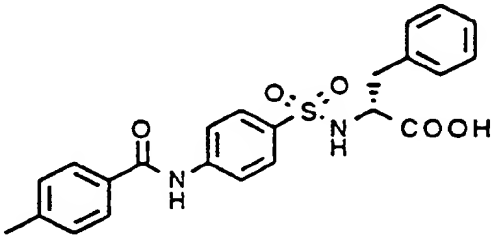
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-aspartic acid



TLC: Rf 0.35 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 10.57 (1H, s), 8.07 (1H, d, J=8.6Hz), 8.0-7.9 (4H, m), 7.76 (2H, d, J=8.8Hz), 7.65-7.5 (3H, m), 4.05 (1H, m), 2.59 (1H, dd, J=6.6, 16.8Hz), 2.40 (1H, dd, J=6.6, 16.8Hz).

Example 2(62)

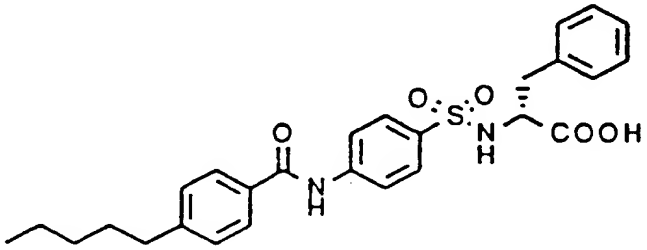
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-phenylalanine



TLC: Rf 0.28 (Chloroform : Methanol : Acetic acid : Water = 100 : 10 : 1 : 1),
NMR (DMSO-d6): δ 12.9-12.4 (1H, br.s), 10.44 (1H, s), 8.17 (1H, d, J=9.2Hz), 7.9-7.8 (4H, m), 7.54 (2H, d, J=8.6Hz), 7.36 (2H, d, J=8.2Hz), 7.3-7.1 (5H, m), 3.9-3.8 (1H, m), 2.93 (1H, dd, J=6.0, 14Hz), 2.72 (1H, dd, J=8.8, 14Hz), 2.40 (3H, s).

Example 2(63)

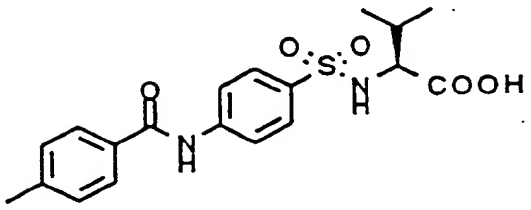
N-[[4-(4-Pentylbenzoylamino)phenyl]sulfonyl]-D-phenylalanine



TLC: Rf 0.21 (Chloroform : Methanol : Acetic acid = 95 : 4 : 1),
NMR (DMSO-d6): δ 13.00-12.20 (1H, br.s), 10.40 (1H, s), 8.11 (1H, d, J=9.0Hz), 7.88 (2H, d, J=8.6Hz), 7.84 (2H, d, J=8.4Hz), 7.52 (2H, d, J=8.6Hz), 7.34 (2H, d, J=8.4Hz). 7.28-7.08 (5H, m), 3.92-3.78 (1H, m), 2.93 (1H, dd, J=5.8, 13.4Hz), 2.71 (1H, dd, J=8.8, 13.4Hz), 2.66 (2H, t, J=8.2Hz), 1.70-1.50 (2H, m), 1.44-1.18 (4H, m), 0.87 (3H, t, J=6.8Hz).

Example 2(64)

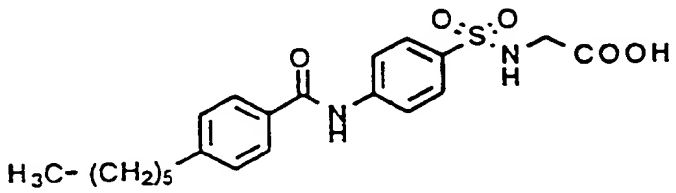
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-L-valine



TLC: Rf 0.45 (Chloroform : Methanol : Acetic acid = 45 : 4 : 1),
NMR (DMSO-d6): δ 12.90-12.30 (1H, br.s), 10.45 (1H, s), 7.94 (1H, br.d, J=9.6Hz), 7.95 (2H, d, J=8.8Hz), 7.88 (2H, d, J=8.2Hz), 7.73 (2H, d, J=8.8Hz), 7.34 (2H. d. J=8.2Hz), 3.49 (1H, dd, J=6.2, 9.6Hz), 2.39 (3H. s), 2.00-1.90 (1H, m), 0.83 (3H, d, J=6.8Hz), 0.80 (3H, d. J=6.8Hz).

Example 2(65)

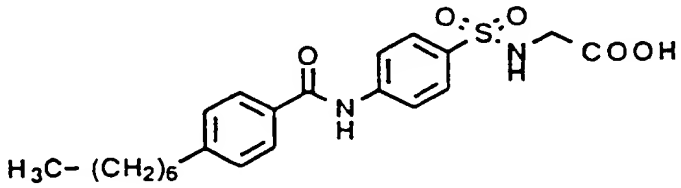
N-[[4-(4-Hexylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.18 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 13.40-12.00 (1H, br.s), 10.46 (1H, s), 7.97 (3H, m), 7.88 (2H, d, J=8.0Hz), 7.87 (1H), 7.75 (2H, d, J=8.8Hz). 7.34 (2H, d. J=8.0Hz), 3.55 (2H, d. J=5.8Hz). 2.66 (2H, t, J=7.8Hz), 1.70-1.50 (2H, m), 1.40-1.15 (6H, m), 0.86 (3H. t J=6.6Hz).

Example 2(66)

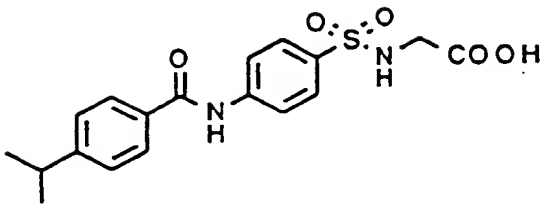
N-[[4-(4-Heptylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.18 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 13.00-12.40 (1H, br.s), 10.48 (1H, s), 7.97 (3H, m), 7.89 (2H, d, J=8.2Hz), 7.87 (1H), 7.77 (2H, d, J=9.0Hz), 7.35 (2H, d, J=8.2Hz), 3.57 (2H, d, J=6.2Hz), 2.66 (2H, t, J=7.8Hz), 1.70-1.44 (2H, m), 1.40-1.10 (8H, m), 0.86 (3H, t. J=7.0Hz).

Example 2(67)

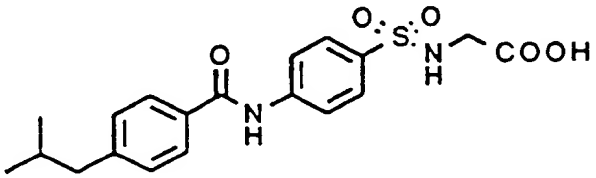
N-[[4-(4-Isopropylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.51 (Chloroform : Methanol : Acetic acid =16 : 3 : 1),
NMR (DMSO-d6): δ 13.20-12.00 (1H, br.s), 10.48 (1H, s), 7.96 (3H, m), 7.89 (2H, d, J=8.2Hz), 7.76 (2H, d, J=8.8Hz), 7.41 (2H, d, J=8.2Hz), 3.57 (2H, d, J=6.0Hz), 2.99 (1H, m), 1.24 (6H, d, J=6.8Hz).

Example 2(68)

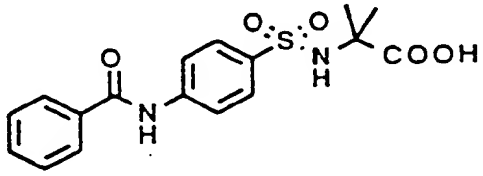
N-[[4-(4-Isobutylbenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.53 (Chloroform : Methanol : Acetic acid =16 : 3 : 1),
NMR (DMSO-d6): δ 13.20-12.00 (1H, br.s), 10.49 (1H, s), 7.96 (3H, m), 7.89 (2H, d, J=8.2Hz), 7.76 (2H, d, J=8.8Hz), 7.33 (2H, d, J=8.2Hz), 3.57 (2H, d, J=6.2Hz), 2.54 (2H, d, J=7.2Hz), 1.88 (1H, m), 0.89 (6H, d, J=6.4Hz).

Example 2(69)

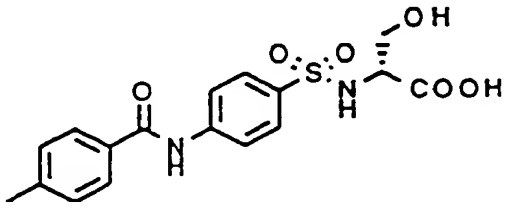
N-[[4-(Benzoylamino)phenyl]sulfonyl]-2,2-dimethylglycine



TLC: Rf 0.14 (Chloroform : Methanol : Acetic acid : Water = 100 : 10 : 1 : 1),
NMR (DMSO-d6): δ 12.55 (1H, br.s), 10.56 (1H, s), 8.0-7.85 (5H, m), 7.77 (2H, d, j=8.8Hz), 7.65-7.5 (3H, m), 1.27 (6H, s).

Example 2(70)

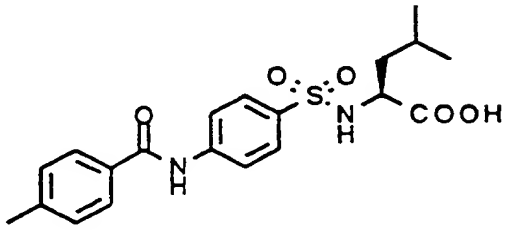
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]amino]-D-serine



TLC: Rf 0.25 (Chloroform : Methanol : Acetic acid =16 : 3 : 1),
NMR (DMSO-d6): δ 13.40-11.60 (1H, br.s), 10.47 (1H. s), 7.95 (2H, d, J=8.8Hz), 7.88 (2H, d, J=8.2Hz), 7.86 (1H, d, J=8.4Hz), 7.75 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.2Hz), 3.80-3.68 (1H, m), 3.53-3.47 (2H), 2.39 (3H, s).

Example 2(71)

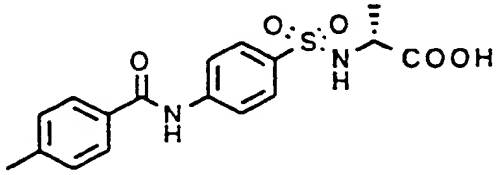
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-L-leucine



TLC: Rf 0.22 (Chloroform : Methanol : Acetic acid : Water = 100 : 10 : 1 : 1),
NMR (DMSO-d6): δ 12.55 (1H, br.s), 10.48 (1H, s), 8.04 (1H, d, J=8.8Hz), 7.96 (2H, d, J=8.8Hz), 7.89 (2H, d, J=8.2Hz), 7.73 (2H, d, J=8.8Hz), 7.36 (2H, d, J=8.2Hz), 3.65 (1H, m), 2.40 (3H, s), 1.59 (1H, m), 1.37 (2H, m), 0.82 (3H, d, J=6.6Hz), 0.72 (3H, d, J=6.4Hz).

Example 2(72)

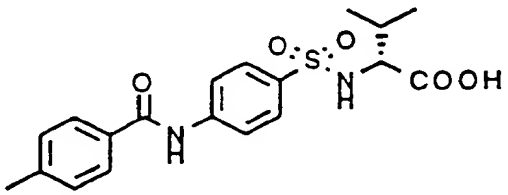
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-alanine



TLC: Rf 0.30 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 13.20-12.00 (1H, br.s), 10.48 (1H, s), 8.02 (1H, d, J=8.2Hz), 7.97 (2H, d, J=8.8Hz), 7.88 (2H, d, J=8.4Hz), 7.75 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.4Hz), 3.82-3.66 (1H, m), 2.39 (3H, s), 1.15 (3H, d, J=7.0Hz).

Example 2(73)

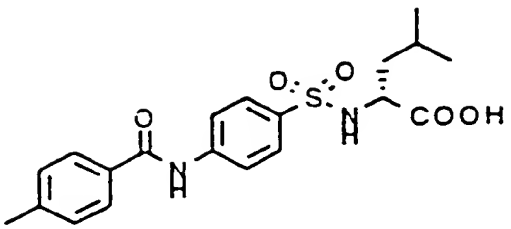
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-valine



TLC: Rf 0.53 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 12.80-12.40 (1H, br.s), 10.46 (1H, s), 7.95 (2H, d, J=8.8Hz), 7.94-7.90 (1H), 7.89 (2H, d, J=8.2Hz), 7.74 (2H, d, J=8.8Hz), 7.35 (2H, d, J=8.2Hz), 3.60-3.45 (1H, m), 2.39 (3H, s), 2.02-1.80 (1H, m), 0.81 (6H, d, J=6.8Hz).

Example 2(74)

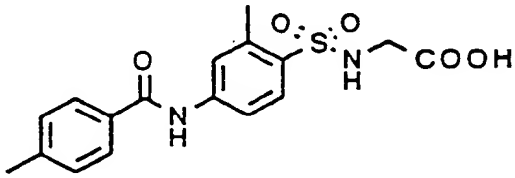
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-leucine



TLC: Rf 0.54 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 12.80-12.30 (1H. br.s), 10.46 (1H, s), 8.02 (1H, d, J=9.0Hz), 7.96 (2H, d, J=8.8Hz), 7.89 (2H, d, J=8.2Hz), 7.73 (2H, d. J=8.8Hz), 7.35 (2H. d. J=8.2Hz), 3.75-3.55 (1H, m), 2.39 (3H, s), 1.70-1.48 (1H, m), 1.46-1.30 (2H. m). 0.82 (3H. d. J=6.6Hz), 0.72 (3H. d. J=6.6Hz).

Example 2(75)

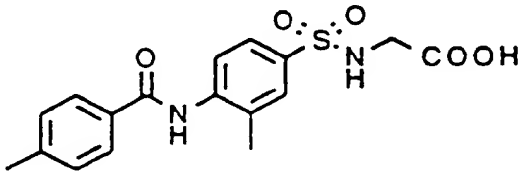
N-[[2-Methyl-4-(p-Toluoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.61 (Chloroform : Methanol = 2 : 1),
NMR (DMSO-d6): δ 10.38 (1H, s), 8.02 (1H, t, J=3.6Hz), 7.88 (2H, d, J=8.1Hz), 7.80-7.77 (3H, m), 7.34 (2H, d, J=8.1 Hz). 3.58 (2H. d. J=3.6Hz), 2.59 (3H. s), 2.40 (3H, s).

Example 2(76)

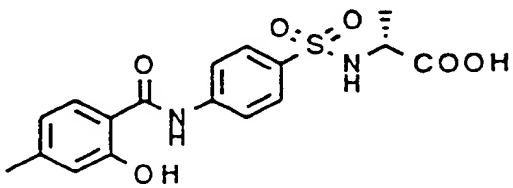
N-[[3-Methyl-4-(p-Toluoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.24 (Chloroform : Methanol = 2 : 1),
NMR (DMSO-d6):δ 12.64 (1H, br.s), 9.88 (1H. s), 7.94 (1H. t, J=6.2Hz), 7.85 (2H, d, J=8.1 Hz), 7.66 (3H, m), 7.30 (2H, d. J=8.1 Hz). 3.55 (2H, d. J=6.2Hz), 2.36 (3H. s). 2.28 (3H. s).

Example 2(77)

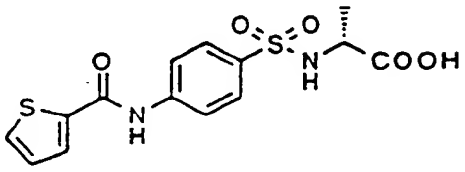
N-[[4-(2-Hydroxy-4-methylbenzoylamino)phenyl]sulfonyl]-D-alanine



TLC: Rf 0.37 (Chloroform : Methanol = 2 : 1),
NMR (DMSO-d6): δ 12.62 (1H, br.s), 11.66 (1H, s), 10.56 (1H, s), 8.06 (1H, d, J=8.6Hz), 7.93-7.70 (5H, m), 6.82 (1H, s), 6.80 (1H, d, J=7.2Hz), 3.76 (1H, m), 2.31 (3H, s), 1.15 (3H, d, J=7.2Hz).

Example 2(78)

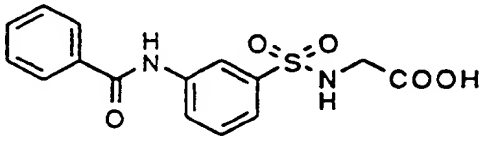
N-[[4-(2-Thienylcarbonylamino)phenyl]sulfonyl]-D-alanine



TLC: Rf 0.21 (Chloroform : Methanol : Water = 4 : 1 : 0.1),
NMR (DMSO-d6): δ 12.60 (1H, br.s), 10.49 (1H, s), 8.05-7.98 (2H, m), 7.91-7.85 (3H, m), 7.73 (2H, d, J=8.8Hz), 7.21 (1H, t, J=3.8Hz), 3.77-3.68 (1H, m), 1.13 (3H, d, J=7.2Hz).

Example 2(79)

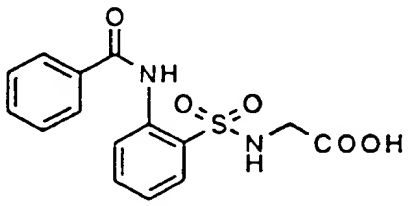
N-[[3-(Benzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.36 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.54 (1H, s), 8.33 (1H, s), 8.14-7.90 (4H, m), 7.68-7.44 (5H, m), 3.60 (2H, d, J=6.0Hz).

Example 2(80)

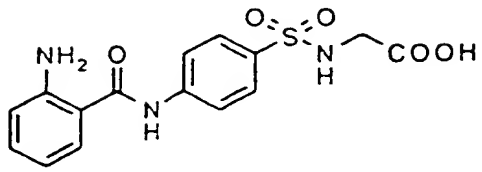
N-[[2-(Benzoylamino)phenyl]sulfonyl]glycine



TLC : Rf 0.34 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 13.00-1 2.60 (1H, br.s), 10.26 (1H, s), 8.67-8.56 (1H), 8.52-8.44 (1H, m), 8.02-7.92 (2H, m), 7.87 (1H, dd, J=1.4, 7.8Hz), 7.74-7.54 (4H, m), 7.38-7.27 (1H, m), 3.65 (2H, d, J=4.6Hz).

Example 3

N-[[4-(2-Aminobenzoylamino)phenyl]sulfonyl]glycine



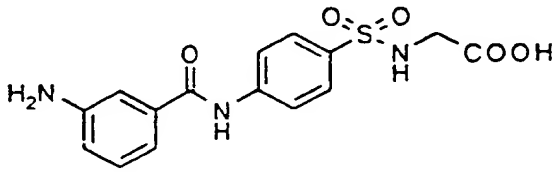
To a solution of the compound prepared in example 2(13) (569 mg) in N, N-dimethylformamide (7.5 ml) and methanol (7.5 ml), 10% palladium carbon (100 mg) and ammonium formate (378 mg) was added. The mixture was stirred for 1 hour at room temperature. The reaction mixture was filtered and the filtrate was concentrated. The residue was washed with water and ether and dried to give the title compound having the following physical data.
TLC: Rf 0.47 (Chloroform :Methanol : acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.60 (1H, br.s), 10.30 (1H, s), 7.95-7.85 (3H, m), 7.74 (2H, d, J=8.8Hz), 7.64 (2H, d, J=8.0Hz), 7.22 (1H, t, J=8.0Hz), 6.76 (1H, d, J=8.0Hz), 6.60 (1H, t, J=8.0Hz), 6.38 (2H, br), 3.56 (2H, d, J=6.2Hz).

Example 3(1)-3(13)

The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 3, using a compound prepared in Example 2(14),
2(15), 2(31), 2(33), 2(40), 2(41), 1(78), 1(79), 1(80), 1(81), 1(82), 1(83) and 1(84) instead of a compound prepared in example 2(13).

Example 3(1)

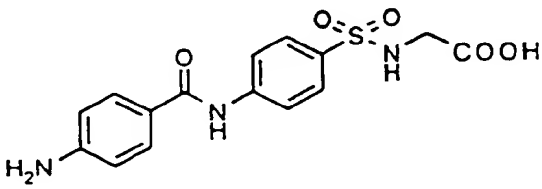
N-[[4-(3-Aminobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.39 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 10.41 (1H, s), 7.85-7.0 (3H, m), 7.74 (2H, d, J=8.4Hz), 7.2-7.05 (3H, m), 6.77 (1H, d, J=7.6Hz), 3.56 (2H, d, J=6.0Hz).

Example 3(2)

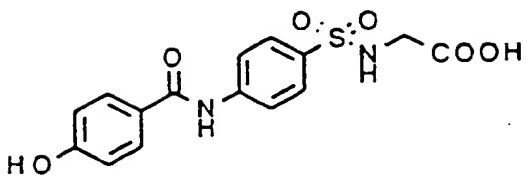
N-[[4-(4-Aminobenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.35 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.60 (1H, br.s), 10.08 (1H, s), 7.94 (2H, d, J=8.8Hz), 7.86 (1H, t, J=6.0Hz), 7.73 and 7.72 (total 4H; each d, both J=8.8Hz), 6.61 (2H, d, J=8.8Hz), 5.83 (2H, br), 3.55 (2H, d, J=6.0Hz).

Example 3(3)

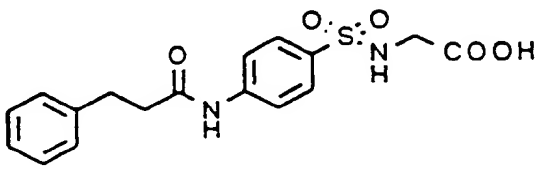
N-[[4-(4-Hydroxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.58 (Chloroform : Methanol : Acetic acid = 20 : 10 : 1),
NMR (DMSO-d6): δ 10.31 (1H, s), 8.01-7.82 (1H, m), 7.95 (2H, d, J=8.8Hz), 7.87 (2H, d, J=8.4Hz), 7.75 (2H, d, J=8.8Hz), 6.88 (2H, d, J=8.4Hz), 3.53 (2H, m).

Example 3(4)

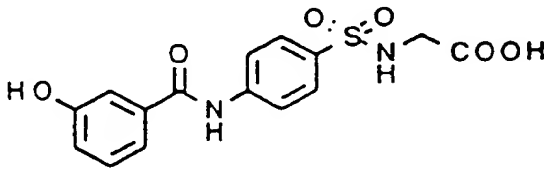
N-[[4-[(2-Phenylethyl)carbonylamino]phenyl]sulfonyl]glycine



TLC: Rf 0.45 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.29 (1H, s), 7.80-7.50 (5H, m), 7.36-7.08 (5H, m), 3.50-3.40 (2H, m), 3.00-2.78 (2H, m), 2.74-2.50 (2H, m).

Example 3(5)

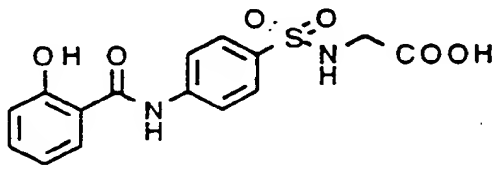
N-[[4-(3-Hydroxybenzoylamino)phenyl]sulfonyl]glycine



TLC: Rf 0.24 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.48 (1H, s), 7.96 (2H, d, J=8.8Hz), 7.95-7.76 (1H, m), 7.75 (2H, d, J=8.8Hz), 7.44-7.28 (3H, m), 7.40-6.95 (1H, m), 3.60-3.50 (2H, m).

Example 3(6)

N-[[4-(2-Hydroxybenzoylamino)phenyl]sulfonyl]glycine

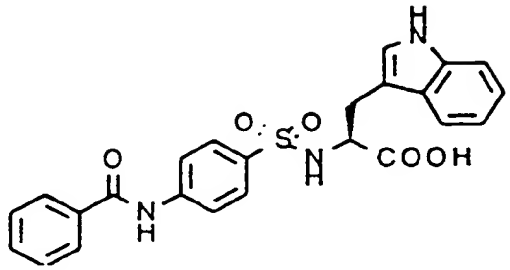


TLC: Rf 0.38 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.20-10.80 (1H, br.s), 10.65 (1H, s), 8.00-7.84 (2H, m), 7.92 (2H, d, J=8.8Hz), 7.78 (2H, d,

J=8.8Hz), 7.44 (1H, m), 7.06-6.92 (2H, m), 3.60-3.48 (2H, m).

Example 3(7)

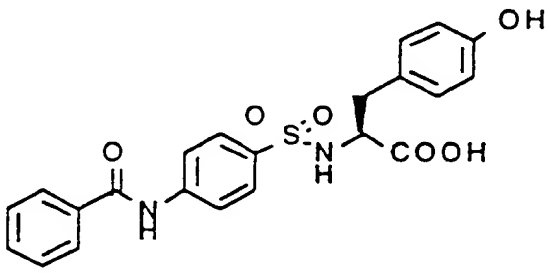
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-tryptophan



TLC: Rf 0.26 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 13.50-11.60 (1H, br,s), 10.78 (1H, s), 10.49 (1H, s), 8.12-8.00 (1H, m), 7.97 (2H, dd, J=1.6, 7.6Hz), 7.85 (2H, d, J=9.0Hz), 7.64-7.49 (5H, m), 7.37-7.25 (2H, m), 7.10-6.86 (3H, m), 4.00-3.80 (1H, m), 3.06 (1H, dd, J=6.6Hz, 14.4Hz), 2.87 (1H, dd, J=7.2, 14.4Hz).

Example 3(8)

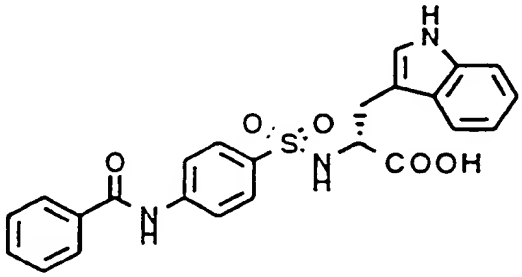
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-tyrosine



TLC: Rf 0.56 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 10.53 (1H, s), 9.25-9.05 (1H, br,s), 8.00-7.93 (3H, m), 7.89 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.8Hz), 7.60-7.48 (3H, m), 6.92 (2H, d, J=8.4Hz), 6.60 (2H, d, J=8.4Hz), 3.80-3.64 (1H, m), 2.80 (1H, dd, J=5.8, 13.6Hz), 2.65 (1H, dd, J=7.6, 13.6Hz).

Example 3(9)

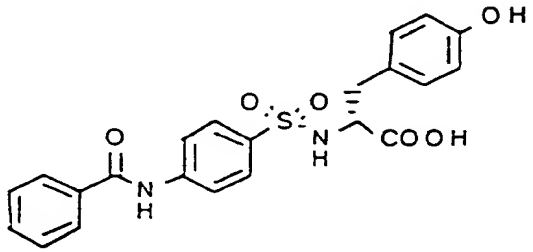
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-tryptophan



TLC: Rf 0.26 (Chloroform : Methanol : Acetic acid = 90 : 10 : 1),
NMR (DMSO-d6): δ 12.80-12.30 (1H. br.s), 10.79 (1H, s), 10.50 (1H, s), 8.09 (1H, d, J=8.6Hz), 8.02-7.93 (2H. m), 7.85 (2H, d, J=8.8Hz), 7.68-7.50 (5H, m), 7.38-7.25 (2H. m), 7.11-6.87 (3H, m), 4.00-3.81 (1H, m), 3.05 (1H, dd, J=6.6, 14.8Hz). 2.86 (1H. dd, J=7.8, 14.8Hz).

Example 3(10)

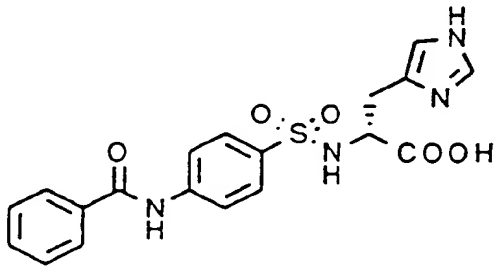
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-tyrosine



TLC: Rf 0.56 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 12.80-12.00 (1H, br.s), 10.54 (1H, s), 9.20 (1H, s), 8.06 (1H, d, J=8.8Hz), 8.02-7.93 (2H, m), 7.89 (2H. d. J=8.8Hz), 7.70-7.50 (5H, m), 6.92 (2H, d, J=8.4Hz), 6.61 (2H, d, J=8.4Hz), 3.90-3.70 (1H, m), 2.81 (1H, dd, J=6.4, 13.6Hz), 2.62 (1H, dd, J=8.2, 13.6Hz).

Example 3(11)

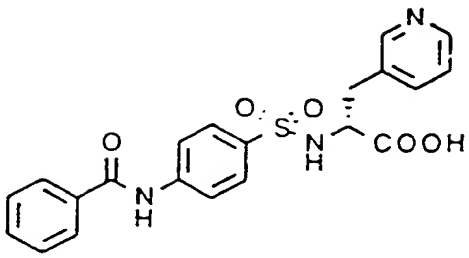
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-histidine



TLC: Rf 0.16 (Chloroform : Methanol : Acetic acid = 14 : 6 : 1),
NMR (DMSO-d6): δ 10.82 (1H, s), 8.29 (1H, s), 8.10 (2H, d, J=9.0Hz), 8.04 (2H, d, J=9.0Hz), 8.00-7.92 (2H, m), 7.68-7.48 (4H, m), 7.45 (1H, s), 3.45-3.35 (1H, m), 3.05 (1H, dd, J=3.6, 15.6Hz), 2.70 (1H, dd, J=9.0, 15.6Hz).

Example 3(12)

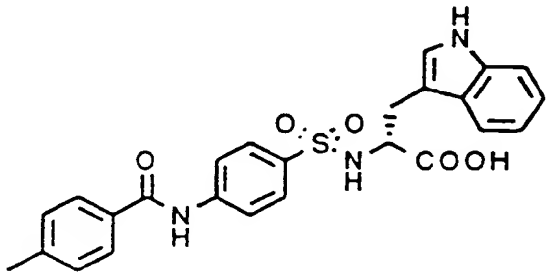
2-[N-[4-(Benzoylamino)phenyl]sulfonylamino]-(3-pyridyl)-D-alanine



TLC: Rf 0.35 (Chloroform : Methanol : Acetic acid = 2 : 1 : 0.1),
NMR (DMSO-d6): δ 12.84 (1H, br.s), 10.54 (1H, s), 8.37 (2H, m), 8.02 (1H, d, J=9.0Hz), 7.96 (2H, m), 7.86 (2H, d, J=8.6Hz), 7.65-7.5 (6H, m), 7.21 (1H, dd, J=4.9, 7.5Hz), 3.89 (1H, m), 3.05-2.7 (2H, m).

Example 3(13)

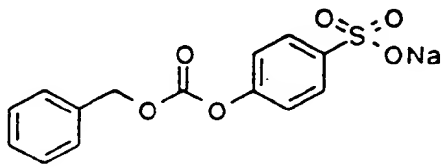
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-tryptophan



TLC: Rf 0.13 (Chloroform : Methanol : Acetic acid : Water = 100 : 10 : 1 : 1),
NMR (DMSO-d6): δ 12.57 (1H, br.s), 10.8 (1H, s), 10.42 (1H, s), 8.13 (1H, d, J=8.8Hz), 7.9-7.8 (4H, m), 7.59 (2H, d, J=8.8Hz), 7.4-7.25 (4H, m), 7.1-6.9 (3H, m), 3.95-3.85 (1H, m), 3.04 (1H, dd, J=6.0, 18.0Hz), 2.84 (1H, dd, J=7.4, 18.0Hz), 2.39 (3H, s).

Reference example 3

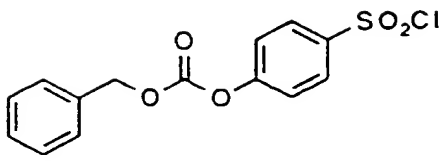
Sodium 4-(Benzyloxycarbonyloxy)benzenesulfonate



To an aqueous solution (40 ml) of sodium hydride (3.8 g), sodium 4-hydroxybenzenesulfonate dihydroxide (20 g) and tetrahydrofuran (28 ml) was added. To the mixture, benzyl chloroformate (12.3 ml) was added at 0°C. The mixture was stirred for 1 hour at 0°C and for 1 hour at room temperature. The reaction mixture was concentrated. The precipitated crystals was washed with water and dried to give the title compound (18.1 g) having the following physical data.
NMR (CD_3OD): δ 7.85 (2H, d, J=8.0Hz), 7-50-7.30 (5H, m), 7.25 (2H, d, J=8.0Hz), 5.25 (2H, s).

Reference example 4

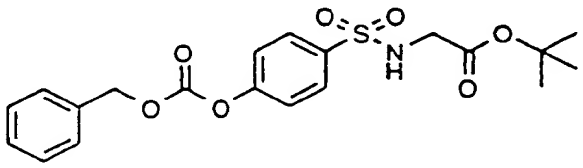
4-(Benzyloxycarbonyloxy)benzenesulfonyl chloride



To a suspension of the compound prepared in reference example 3 (10.2 g) in N, N-dimethylformamide (30 ml), sulfonyl chloride (3.4 ml) was added at 0°C. The mixture was stirred for 1 hour at room temperature. The reaction mixture was poured into ice-water (50 ml). The precipitated crystals was washed with water and dried to give the title compound (9.6 g) having the following physical data.
NMR (CD_3OD) : δ 8.10 (2H, d, J=8.0Hz), 7.50 (2H, d, J=8.0Hz), 7.45-7.40 (5H, m), 5.30 (2H, s).

Example 4

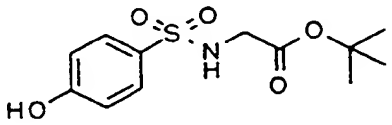
N-[[4-(Benzyloxycarbonyloxy)phenyl]sulfonyl]glycine t-butyl ester



To a solution of glycine t-butyl ester hydrochloride (1.5 g) in pyridine (20 ml), a compound prepared in reference example 4 (3.0 g) was added. The mixture was stirred overnight at room temperature. The reaction mixture was concentrated and the residue was dissolved into ethyl acetate. The solution was washed with 1N hydrochloric acid, water and a saturated aqueous solution of sodium chloride, dried over anhydrous magnesium sulfate and concentrated to give the title compound (2.4 g) having the following physical data.
TLC: Rf 0.78 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$) : δ 7.90 (2H, d, J=8.0Hz), 7.50-7.30 (5H, m), 7.35 (2H, d, J=8.0Hz), 5.30 (2H, s), 5.05 (1H, t, J=6.0Hz), 3.70 (2H, d, J=6.0Hz), 1.40 (9H, s).

Reference example 5

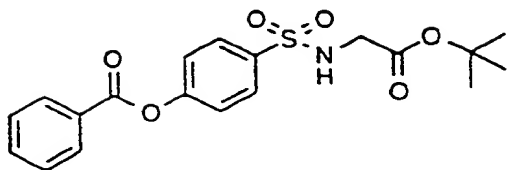
N-[4-(Hydroxyphenyl)sulfonyl]glycine t-butyl ester



To a solution of a compound prepared in example 4 (2.3 g) in ethanol (50 ml), 10% palladium carbon (200 mg) was added. The mixture was stirred for 2 hours at room temperature under an atmosphere of hydrogen. The reaction mixture was filtered through celite (registered trade mark). The filtrate was concentrated. The residue was purified by column chromatography on silica gel (hexane : ethyl acetate = 3 : 1 → 2 : 1) to give the title compound (1.5 g) having the following physical data.
TLC: Rf 0.19 (Hexane : Ethyl acetate = 2 : 1),
NMR ($CDCl_3$) :δ 7.70 (2H, d, J=8.0Hz), 6.90 (2H, d, J=8.0Hz), 3.75 (1H, br.s), 3.60 (2H, br.s), 1.40 (9H, s).

Example 5

N-[[4-(Benzoyloxy)phenyl]sulfonyl]glycine t-butyl ester



The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 1, using a compound prepared in reference Example 5 instead of a compound prepared in reference Example 2, and benzoyl chloride instead of p-toluoyl chloride.

TLC: Rf 0.62 (Hexane : Ethyl acetate = 1 : 1),

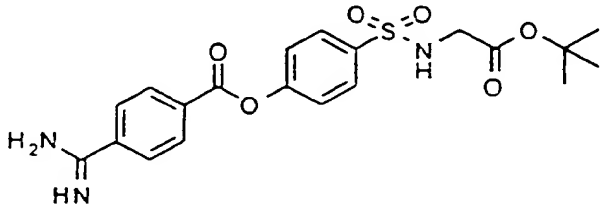
NMR ($CDCl_3$): δ 8.20 (2H, d, J=7.2Hz), 7.95 (2H, d, J=9.0Hz), 7.68 (1H, t, J=7.2Hz), 7.54 (2H, t, J=7.2Hz), 7.39 (2H, d, J=9.0Hz), 5.07 (1H, t, J=5.2Hz), 3.71 (2H, d, J=5.2Hz), 1.39 (9H, s).

Example 5(1)-5(6)

The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 4, using a corresponding amino acid ester derivative instead of glycine t-butyl ester hydrochloride, and then by the same procedure as a series of reactions of Reference Example 5, and then by the same procedure as a series of reactions of Example 5, using a corresponding acyl chloride derivative or a corresponding carboxylic acid derivative and a condensing agent (e.g. 1,3-dicyclohexylcarbodiimide (DCC), 1-ethyl-3-[3-(dimethylamino)propyl] carbodiimide (EDC)) instead of benzoyl chloride, or converting to a corresponding salt by conventional method.

Example 5(1)

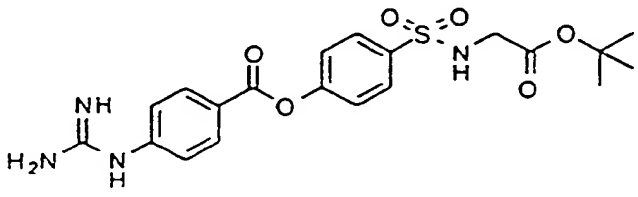
N-[[4-(4-Amidinobenzoyloxy)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.41 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1).

Example 5(2)

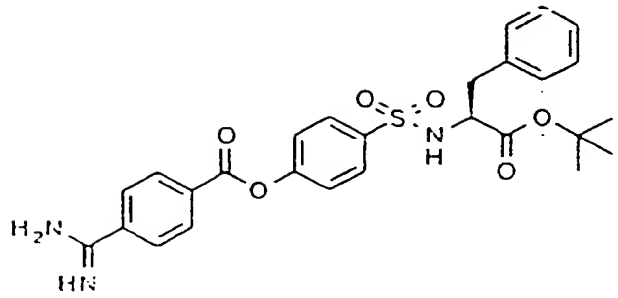
N-[[4-(4-Guanidinobenzoyloxy)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.35 (Chloroform : Methanol : acetic acid = 10 : 2 : 1).

Example 5(3)

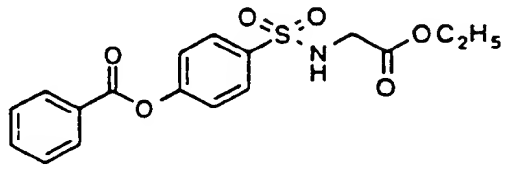
N-[[4-(4-Amidinobenzoyloxy)phenyl]sulfonyl]-L-phenylalanine t-butyl ester



TLC: Rf 0.43 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1).

Example 5(4)

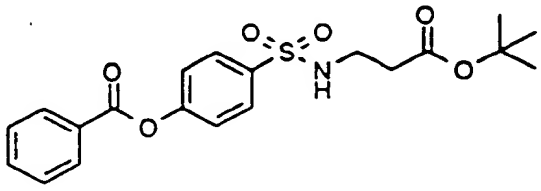
N-[[4-(Benzoyloxy)phenyl]sulfonyl]glycine ethyl ester



TLC: Rf 0.44 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.20 (2H, d, J=7.0Hz), 7.95 (2H, d, J=8.7Hz), 7.68 (1H, m), 7.53 (2H, m), 7.40 (2H, d, J=8.7Hz), 5.11 (1H, t, J=5.4Hz), 4,13 (2H, q, J=7.1Hz), 3.82 (2H, d, J=5.4Hz), 1.23 (3H, t, J=7.1 Hz).

Example 5(5)

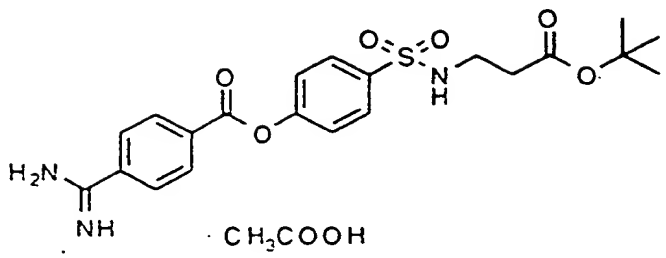
N-[[4-(Benzoyloxy)phenyl]sulfonyl]-β-alanine t-butyl ester



TLC : Rf 0.77 (Ethyl acetate),
NMR ($CDCl_3$): δ 8.21 (2H, d, J=8.0Hz), 7.95 (2H, d, J=9.0Hz), 7.68 (1H, t, J=8.0Hz), 7.54 (2H, t, J=8.0Hz), 7.40 (2H, d, J=9.0Hz), 5.31 (1H, t, J=6.0Hz), 3.19 (2H, q, J=6.0Hz), 2.49 (2H, t, J=6.0Hz), 1.44 (9H, s).

Example 5(6)

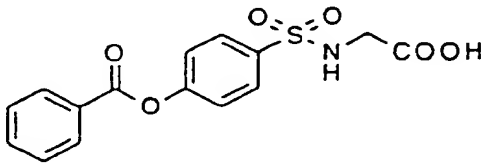
N-[[4-(4-Amidinobenzoyloxy)phenyl]sulfonyl]-β-alanine t-butyl ester acetate



TLC : Rf 0.36 (Chloroform : Methanol Acetic acid = 10 : 2 : 1).

Example 6

N-[[4-(Benzoyloxy)phenyl]sulfonyl]glycine



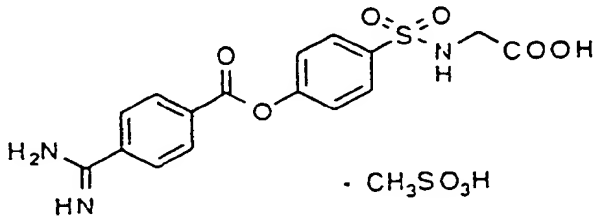
The title compound haying the following physical data were obtained by the same procedure as a series of reactions of Example 2, using a compound prepared in Example 5 instead of a compound prepared in Example 1.
TLC : Rf 0.12 (Chloroform : Methanol : Water = 90 : 10 : 1),
NMR ($CDCl_3$+CD_3OD):δ 8.16 (2H. d. J=7.6Hz), 7.93 (2H, d, J=9.0Hz), 7.66 (1H, t, J=7.6Hz), 7.55 (2H, t, J=7.6Hz), 7.34 (2H. d. J=9.0Hz), 3.77 (2H, S).

Example 6(1)-6(5)

The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 6, if necessary, by converting to corresponding salts by conventional method, using a compound prepared in Example 5(1)-5(3), 5(5) and 5(6)instead of a compound prepared in example 5.

Example 6(1)

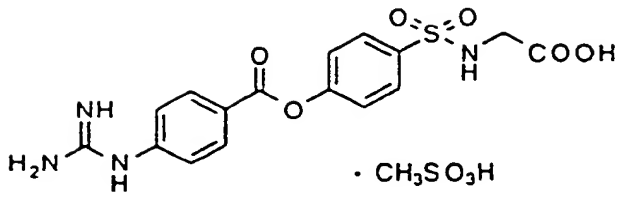
N-[[4-(4-Amidinobenzoyloxy)phenyl]sulfonyl]glycine methansulfonate



TLC: Rf 0.27 (Chloroform : Methanol : Acetic acid = 3 : 1 : 1),
NMR (DMSO-d6): δ 9.55 (2H, br.), 9.35 (2H, br.), 8.35 (2H, d, J=8.0Hz), 8.00 (2H, d, J=8.0Hz), 7.95 (d, J=9.0Hz), 7.60 (2H. d. J=9.0Hz), 3.60 (2H, br.), 3.40 (1H, br.), 2.40 (6H, s).

Example 6(2)

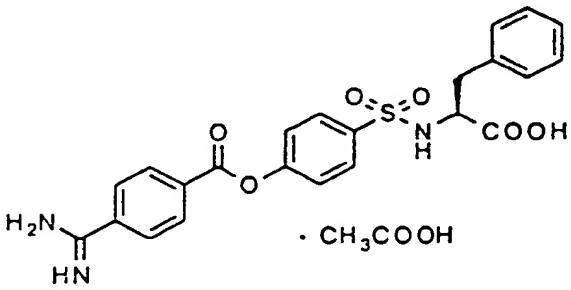
N-[[4-[[(4-Guanidinobenzoyloxy)phenyl]sulfonyl]glycine methansulfonate



TLC: Rf 0.45 (Chloroform : Methanol : Acetic acid = 3 : 1 : 1),
NMR (CD_3OD): δ 8.25 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 7.45 (2H, d, J=8.0Hz), 7.43 (2H, d, J=8.0Hz), 3.73 (2H, s), 2.69 (3H, s).

Example 6(3)

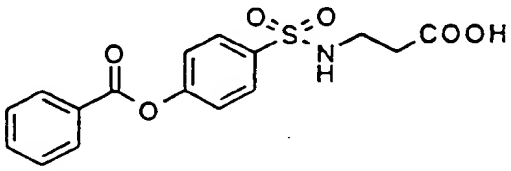
N-[[4-[[(4-Amidinobenzoyloxy)phenyl]sulfonyl]-L-phenylalanine acetate



TLC: Rf 0.24 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3COOD): δ 8.40 (2H, d, J=7.5Hz), 8.05 (2H, d, J=7.5Hz), 7.80 (2H, d, J=8.0Hz), 7.35 (2H, d, J=8.0Hz), 7.30-7.15 (5H, m), 4.30 (1H, t, J=6.0Hz), 3.20 (1H, dd, J=15, 6.0Hz), 2.95 (1H, dd, J=15, 6.0Hz).

Example 6(4)

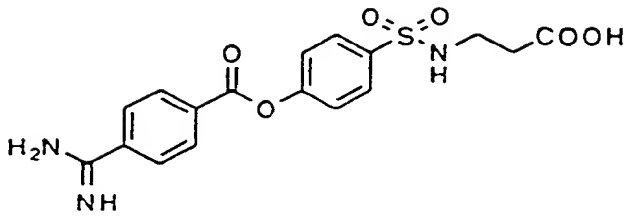
N-[[4-(Benzoyloxy)phenyl]sulfonyl]-β-alanine



TLC : Rf 0.36 (Chloroform : Methanol : Acetic acid : Water = 100 : 10 : 1 : 1),
NMR ($CDCl_3$ + CD_3OD): δ 8.20 (2H, d, J=7.0Hz), 7.95 (2H, d, J=9.0Hz), 7.69 (1H, t, J=7.0Hz), 7.55 (2H, t, J=7.0Hz), 7.40 (2H, d, J=9.0Hz), 3.22 (2H, t, J=6.0Hz), 2.55 (2H, t, J=6.0Hz).

Example 6(5)

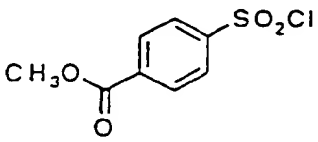
N-[[4-(4-Amidinobenzoyloxy)phenyl]sulfonyl]-β-alanine



TLC : Rf 0.176 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3COOD) : δ 8.40 (2H, d, J=7.5Hz), 8.05 (2H, d, J=7.5Hz), 8.00 (2H, d, J=8.0Hz), 7.50 (2H, d, J=8.0Hz), 3.25 (2H, t, J=6.0Hz), 2.60 (2H, t, J=6.0Hz).

Reference example 6

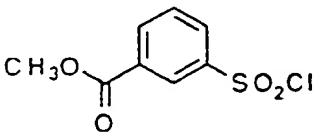
4-(Methoxycarbonyl)benzenesulfonyl chloride



A suspension of 4-Carboxybenzenesulfonyl chloride (2.2 g) in thionyl chloride (10 ml) was refluxed for 1 hour. The reaction mixture was cooled to room temperature and concentrated. The residue was dissolved in methanol (10 ml), and stirred for 1 hours at room temperature. The reaction mixture was concentrated to give the title compound (2.3 g).

Reference example 7

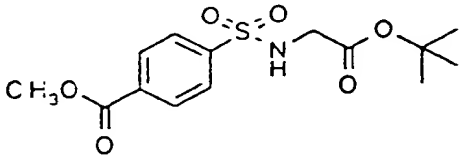
3-(Methoxycarbonyl)benzenesulfonyl chloride



The title compound was obtained by the same procedure as a series of reactions of reference example 6, using 3-carboxybenzenesulfonyl chloride instead of 4-carboxybenzenesulfonyl chloride.

Example 7

N-[[4-(Methoxycarbonyl)phenyl]sulfonyl]glycine t-butyl ester



The title compound having the following physical data was obtained by the same procedure as a series of reactions of Example 4, using a compound prepared in reference Example 6 instead of a compound prepared in reference Example 4.

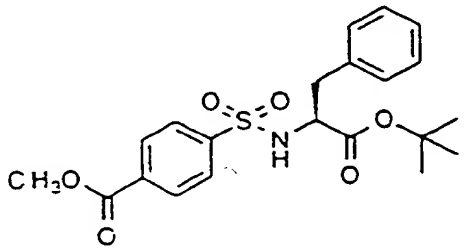
TLC: Rf 0.56 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$):δ 8.16 (2H, d, J=8.8Hz), 7.93 (2H, d, J=8.8Hz), 5.09 (1H, t, J=5.4Hz), 3.95 (3H, s), 3.70 (2H, d, J=5.4Hz), 1.34 (9H, s).

Example 7(1)-7(8)

The compounds haying the following physical data were obtained by the same procedure as a series of reactions of Example 7, using a compound prepared in reference Example 6 or 7, and a corresponding amino acid.

Example 7(1)

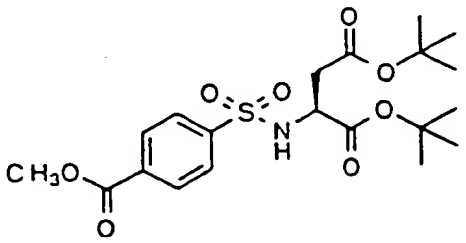
N-[[4-(Methoxycarbonyl)phenyl]sulfonyl]-L-phenylalanine t-butyl ester



TLC: Rf 0.59 (Hexane : Ethyl acetate = 2 : 1),
NMR ($CDCl_3$): δ 8.10 (2H, d, J=8.0Hz), 7.80 (2H, d, J=8.0Hz), 7.30-7.20 (3H, m), 7.20-7.10 (2H, m), 5.15 (1H, d, J=9.0Hz), 4.10 (1H, m), 3.95 (3H, s), 3.00 (2H, d, J=6.0Hz), 1.20 (9H, s).

Example 7(2)

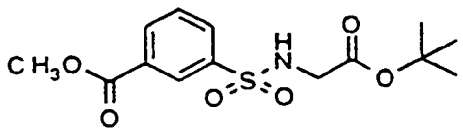
N-[[4-(Methoxycarbonyl)phenyl]sulfonyl]-L-aspartic acid di-t-butyl ester



TLC: Rf 0.64 (Hexane : Ethyl acetate = 2 : 1),
NMR ($CDCl_3$):δ 8.10 (2H, d, J=8.0Hz), 7.90 (2H, d, J=8.0Hz), 5.65 (1H, d, J=9,0Hz), 3.95 (1H, m), 3.90 (3H, s), 2.75 (1H, dd, J=15, 5.0Hz), 2.65 (1H, dd, J=15, 5.0Hz), 1.35 (9H, s), 1.25 (9H, s).

Example 7(3)

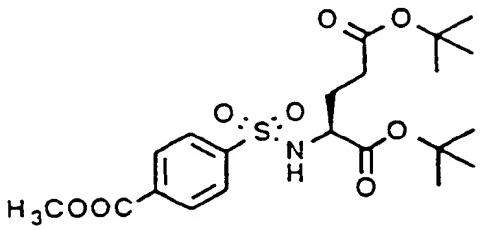
N-[[3-(Methoxycarbonyl)phenyl]sulfonyl]glycine t-butyl ester



TLC: Rf 0.45 (Hexane : Ethyl acetate = 2 : 1).

Example 7(4)

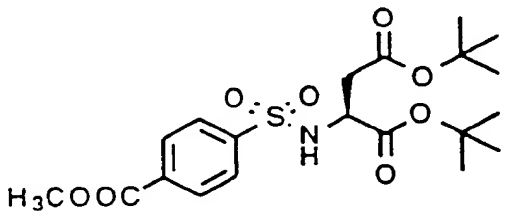
N-[(4-Methoxycarbonylphenyl)sulfonyl]-L-glutamic acid di-t-butyl ester



TLC: Rf 0.59 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.14 (2H, d, J=9.0Hz), 7.90 (2H, d, J=9.0Hz), 5.31 (1H, d, J=9.0Hz), 3.96 (3H, s), 3.92-3.80 (1H, m), 2.43-2.35 (2H, m), 2.16-1.98 (1H, m), 1.88-1.66 (1H, m), 1.46 (9H, s), 1.24 (9H, s).

Example 7(5)

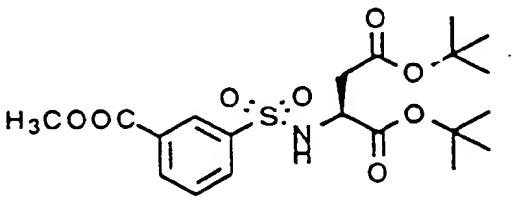
N-[(4-Methoxycarbonylphenyl)sulfonyl]-L-aspanic acid di-t-butyl ester



TLC: Rf 0.83 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.15 (2H, d, J=9.0Hz), 7.94 (2H, d, J=9.0Hz), 5.72 (1H, d, J=9.0Hz), 4.08-4.00 (1H, m), 3.96 (3H, s), 2.91-2.65 (2H, m), 1.43 (9H, s), 1.30 (9H, s).

Example 7(6)

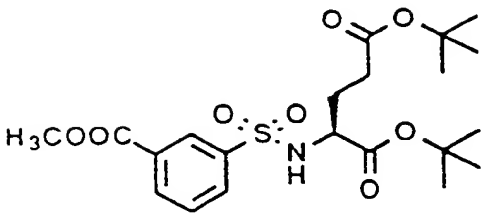
N-[(3-Methoxycarbonylphenyl)sulfonyl]-L-aspartic acid di-t-butyl ester



TLC: Rf 0.33 (Hexane : Ethyl acetate = 8 : 2),
NMR ($CDCl_3$): δ 8.51 (1H, t, J=2.0Hz), 8.24 (1H, dt, J=8.0Hz, 2Hz), 8.06 (1H, dt, J=8.0Hz, 2Hz), 7.60 (1H, t, J=8.0Hz), 5.73 (1H, d, J=9.0Hz), 4.10-4.01 (1H, m), 3.96 (3H, s), 2.91-2.66 (2H, m), 1.41 (9H, s), 1.27 (9H, s).

Example 7(7)

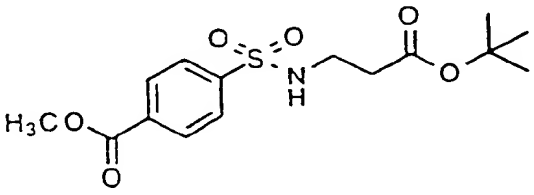
N-[(3-Methoxycarbonylphenyl)sulfonyl]-L-glutamic acid di-t-butyl ester



TLC: Rf 0.33 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 8.48 (1H, t, J=2.0Hz), 8.23 (1H, dt, J=8.0Hz, 2Hz), 8.02 (1H, dt, J=8.0Hz, 2Hz), 7.59 (1H, t, J=8.0Hz), 5.32 (1H, d, J=9.0Hz), 3.96 (3H, s), 3.92-3.81 (1H, m), 2.40 (2H, t, J=8.0Hz), 2.13-1.96 (1H, m),1.87-1.66 (1H, m), 1.46 (9H, s), 1.23 (9H, s).

Example 7(8)

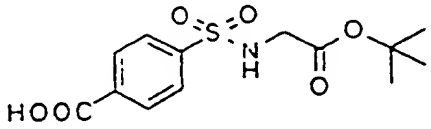
N-[4-(Methoxycarbonylphenyl)sulfonyl]-β-alanine t-butyl ester



TLC : Rf 0.43 (Hexane : Ethyl acetate = 2 : 1),
NMR ($CDCl_3$): δ 8.20 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 5.40 (1H, t, J=6.0Hz), 4.00 (3H, s), 3.20 (2H, dt, J=6.0Hz, 6.0Hz), 2.50 (3H, t, J=6.0Hz), 1.45 (9H, s).

Example 8

N-[(4-Carboxyphenyl)sulfonyl]glycine t-butyl ester



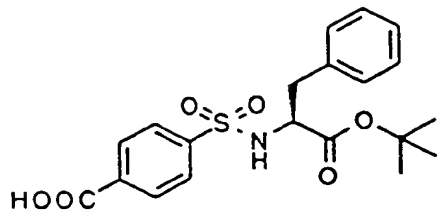
To a solution of a compound prepared in Example 7 (658 mg) in methanol (2 ml) and dioxane (2 ml), 5N aqueous solution of sodium hydroxide (0.8 ml) was added. The mixture was stirred for one day at room temperature. The reaction mixture was neutralized by adding 2N hydrochloric acid and extracted with ethyl acetate. The extract was dried over anhydrous magnesium sulfate and concentrated. The residue was purified by column chromatography on silica gel (methylene chloride : methanol : acetic acid : water = 100 : 10 : 1 : 1) to give the title compound (333 mg) having the following physical data.
TLC: Rf 0.49 (Chloroform : Methanol : Acetic acid : Water = 90 : 10 : 1 : 1),
NMR (CD_3OD): δ 8.16 (2H, d, J=8.8Hz), 7.94 (2H, d, J=8.8Hz), 3.69 (2H, s), 1.31 (9H, s).

Example 8(1)-8(8)

The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 8, using a compound prepared in Example 7(1)-7(8) instead of a compound prepared in Example 7.

Example 8(1)

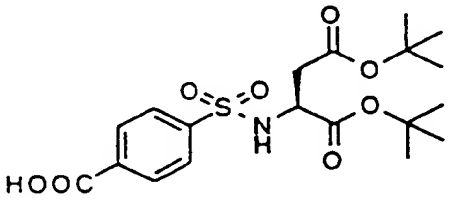
N-[(4-Carboxypheny)sulfonyl]-L-phenylalanine t-butyl ester



TLC: Rf 0.25 (Chloroform : Methanol = 9 : 1),
NMR ($CDCl_3$): δ 8.15 (2H, d, J=8.0Hz), 7.85 (2H, d, J=8.0Hz), 7.30-7.20 (3H, m), 7.20-7.10 (2H, m), 5.30 (1H, d, J=9.0Hz), 4.15 (1H, m), 3.00 (2H, d, J=6.0Hz), 1.25 (9H. s).

Example 8(2)

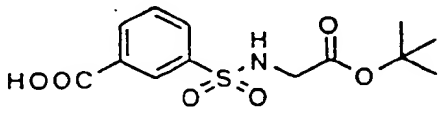
N-[(4-Carboxypheny)sulfonyl]-L-aspartic acid di-t-butyl ester



TLC: Rf 0.28 (Chloroform : Methanol = 9 :1),
NMR ($CDCl_3$):δ 8.20 (2H, d, J=8.0Hz), 8.00 (2H, d, J=8.0Hz), 5.80 (1H, d, J=9.0Hz), 4.05 (1H, m), 2.80 (2H, m), 1.40 (9H. s), 1.30 (9H. s).

Example 8(3)

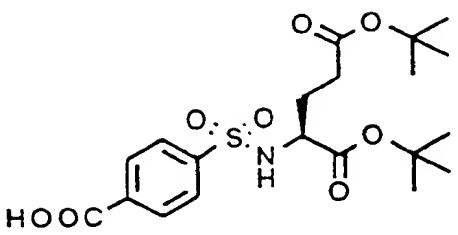
N-[(3-Carboxypheny)sulfonyl]glycine t-butyl ester



TLC: Rf 0.22 (Chloroform : Methanol = 9 : 1).

Example 8(4)

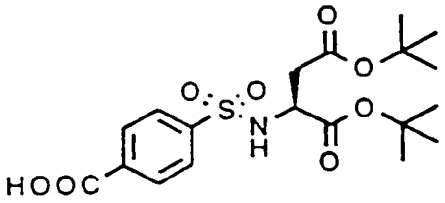
N-[4-(Carboxypheny)sulfonyl]-L-glutamic acid di-t-butyl ester



TLC: Rf 0.25 (Chloroform : Methanol = 9 : 1),
NMR ($CDCl_3$): δ 8.30-8.10 (2H, br.d, J=8.0Hz), 8.10-7.80 (2H, br.d, J=8.0Hz), 5.50-5.30 (1H, br.d, J=9.0Hz), 4.00-3.78 (1H, m), 2.50-1.60 (8H, m), 1.43 (9H, s), 1.23 (9H, s).

Example 8(5)

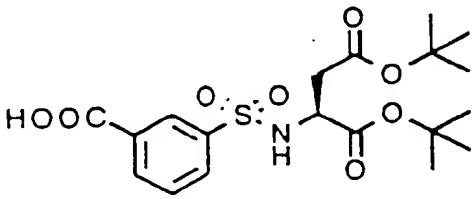
N-[(4-Carboxypheny)sulfonyl]-L-aspartic acid di-t-butyl ester



TLC: Rf 0.30 (Chloroform : Methanol = 9 : 1),
NMR ($CDCl_3$): δ 8.22-8.04 (2H, br.d, J=8.0Hz), 7.96-7.76 (2H, br.d, J=8.0Hz), 6.00-5.82 (1H, br.d, J=9.0Hz), 4.16-4.00 (1H, m), 2.92-2.63 (2H, m), 1.40 (9H, s), 1.25 (9H, s).

Example 8(6)

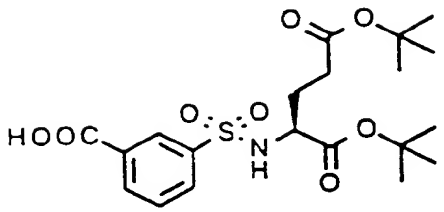
N-[(3-Carboxypheny)sulfonyl]-L-aspartic acid di-t-butyl ester



TLC: Rf 0.46 (Chloroform : Methanol : Water = 8 : 2 : 0.1),
NMR ($CDCl_3$): δ 8.63 (1H, t, J=2.0Hz), 8.29 (1H, dt, J=8.0Hz,2.0Hz), 8.12 (1H, dt, J=8.0Hz, 2.0Hz), 7.64 (1H, t, J=8.0Hz), 6.00 (1H, d, J=9.0Hz), 4.16-4.07 (1H, m), 2.94-2.69 (2H, m), 1.43 (9H, s), 1.28 (9H, s).

Example 8(7)

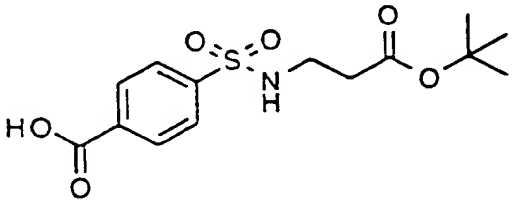
N-[(3-Carboxypheny)sulfonyl]-L-glutamic acid di-t-butyl ester



TLC: Rf 0.54 (Chloroform : Methanol : Water = 8 · 2 : 0.1),
NMR ($CDCl_3$): δ 8.57 (1H, t, J=2.0Hz), 8.29 (1H, dt, J=8.0Hz, 2.0Hz), 8.08 (1H, dt, J=8.0Hz, 2.0Hz), 7.63 (1H, t, J=8.0Hz), 5.61 (1H, d, J=9.0Hz), 3.97-3.86 (1H, m), 2.42 (2H, t, J=7.0Hz), 2.15-1.98 (1H, m), 1.90-1.72 (1H, m), 1.47 (9H, s), 1.25 (9H, s).

Example 8(8)

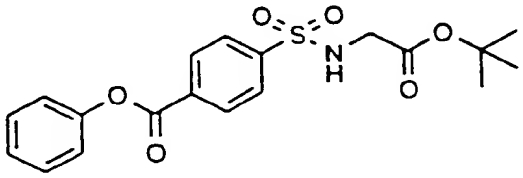
N-[(Carboxyphenyl)sulfonyl]-β-alanine t-butyl ester



TLC : Rf 0.31 (Chloroform : Methanol = 4 : 1),
NMR ($CDCl_3$): δ 8.20 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 3.20 (2H, t, J=6.0Hz), 2.45 (2H, t, J=6.0Hz), 1.45 (9H, s).

Example 9

N-[[4-(Phenoxycarbonyl)phenyl]sulfonyl]glycine t-butyl ester



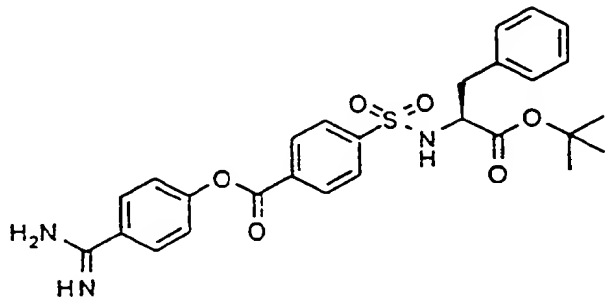
To a solution of a compound prepared in example 8 (221 mg) in pyridine (3.5 ml), phenol (79 mg), N, N-dimethylaminopyridine (9 mg) and dicyclohexylcarbodiimide (159 mg) were added successively. The mixture was stirred overnight and concentrated. The residue was purified by column chromatography on silica gel (hexane : ethyl acetate = 5 : 1) to give the title compound having the following physical data.
TLC: Rf 0.77 (Ethyl acetate),
NMR ($CDCl_3$): δ 8.35 (2H, d, J=8.8Hz), 8.02 (2H, d, J=8.8Hz), 7.47 (2H, t, J=6.0Hz), 7.31 (1H, t, J=6.0Hz), 7.22 (2H, d, J=6.0Hz), 5.16 (1H, t, J=5.4Hz), 3.74 (2H, d, J=5.4Hz), 1.37 (9H, s).

Example 9(1)-9(10)

The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 9, if necessary, by converting to corresponding salts by conventional method using a compound prepared in Example 8 and 8(1)-8(8) and a corresponding alcohol and amine.

Example 9(1)

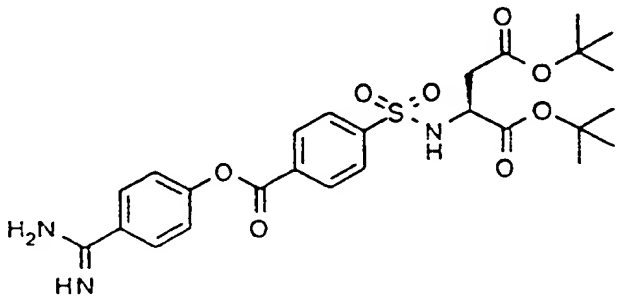
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-L-phenylalanine t-butyl ester



TLC : Rf 0.45 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD):δ 8.25 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 7.85 (2H, d, J=8.0Hz), 7.55 (2H, d, J=8.0Hz), 7.25-7.10 (5H, m), 4.00 (1H, t, J=7.5Hz), 3.00 (1H, dd, J=15.0, 7.5Hz), 2.85 (1H, dd, J=15.0, 7.5Hz), 1.25 (9H, s).

Example 9(2)

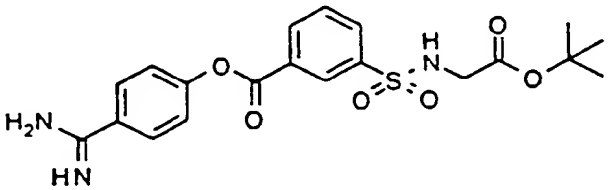
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-L-aspanic acid di-t-butyl ester



TLC : Rf 0.51 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD):δ 8.35 (2H, d, J=8.0Hz), 8.05 (2H, d, J=8.0Hz), 7.95 (2H, d, J=9.0Hz), 7.55 (2H, d, J=9.0Hz), 4.20 (1H, m), 2.60 (2H, m), 1.45 (9H, s), 1.30 (9H, s).

Example 9(3)

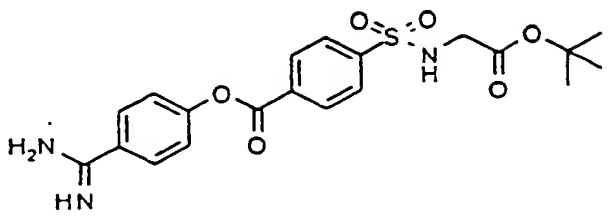
N-[[3-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]glycine t-butyl ester



TLC : Rf 0.33 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD): δ 8.60 (1H, s), 8.40 (1H, d, J=8.0Hz), 8.20 (1H, d, J=8.0Hz), 7.95 (2H, d, J=9.0Hz), 7.80 (1H, t, J=8.0Hz), 7.55 (2H, d, J=9.0Hz), 3.75 (2H, s), 1.35 (9H, s).

Example 9(4)

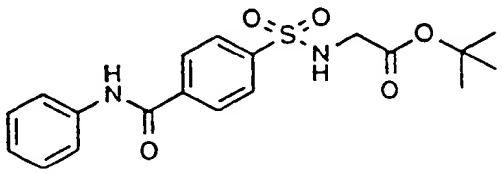
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]glycine t-butyl ester



TLC : Rf 0.45 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD):δ 8.35 (2H, d, J=8.0Hz), 8.05 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 7.55 (2H, d, J=8.0Hz), 3.75 (2H, s), 1.40 (9H, s).

Example 9(5)

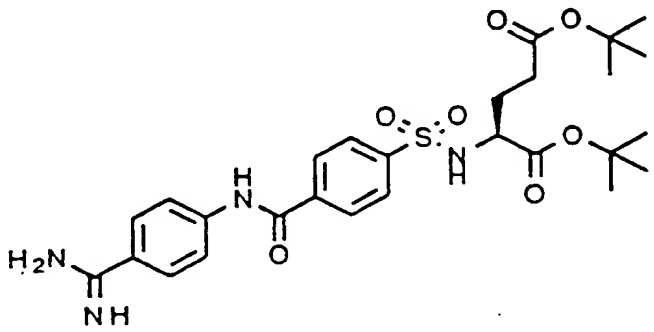
N-[[4-(N-Phenylcarbamoyl)phenyl]sulfonyl]glycine t-butyl ester



TLC : Rf 0.40 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$+CD_3OD): δ 8.04 (2H, d, J=8.8Hz), 7.95 (2H,d,J=8.8Hz), 7.69 (2H, d, J=8.0Hz), 7.39 (2H, t, J=8.0Hz), 7.18 (1H, t. J=8.0Hz), 3.70 (2H, s), 1.36 (9H, s).

Example 9(6)

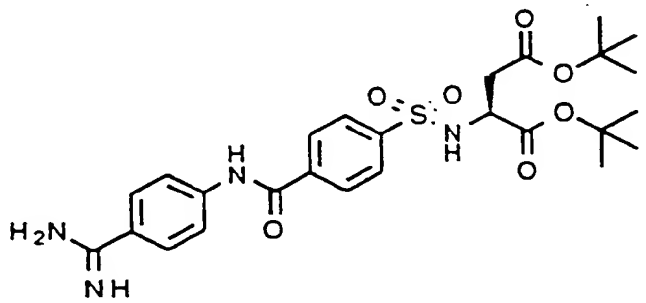
N-[[4-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-glutamic acid di-t-butyl ester



TLC : Rf 0.59 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD): δ 8.07 (2H, d, J=9.0Hz), 7.99 (2H, d, J=8.0Hz), 7.93 (2H, d, J=9.0Hz), 7.80 (2H, d, J=8.0Hz), 3.84 (1H, m), 2.35-2.23 (2H, m), 2.03-1.85 (1H, m), 1.76-1.55 (1H, m), 1.39 (9H, s), 1.21 (9H, s).

Example 9(7)

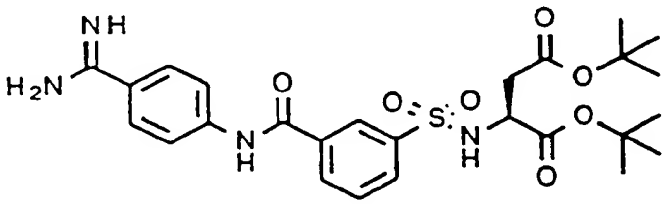
N-[[4-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-aspartic acid di-t-butyl ester



TLC : Rf 0.59 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD): δ 8.12 (2H, d, J=9.0Hz), 8.04 (2H, d, J=8.0Hz), 8.01 (2H, d, J=9.0Hz), 7.85 (2H, d, J=8.0Hz), 4.18 (1H, dd, J=7.0Hz, 6.0Hz), 2.70 (1H, dd, J=16Hz, 6.0Hz), 2.57 (1H, dd, J=16Hz, 7Hz), 1.44 (9H, s), 1.29 (9H, s).

Example 9(8)

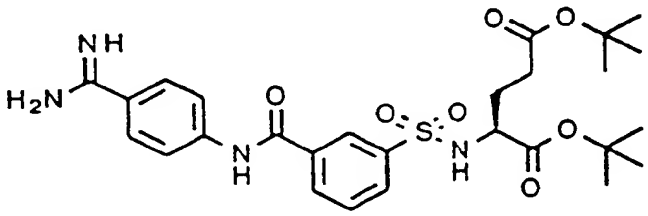
N-[[3-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-aspartic acid di-t-butyl ester



TLC : Rf 0.59 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD): δ 8.45 (1H, s), 8.20 (1H, d, J=8.0Hz), 8.09 (1H, d, J=8.0Hz), 8.05 (2H, d, J=9.0Hz), 7.86 (2H, d, J=9.0Hz), 7.73 (1H, t, J=8.0Hz), 4.21 (1H, dd, J=7.0Hz, 6.0Hz), 2.70 (1H, dd, J=16Hz, 6.0Hz), 2.57 (1H, dd, J=16Hz, 7Hz), 1.43 (9H, s), 1.27 (9H, s).

Example 9(9)

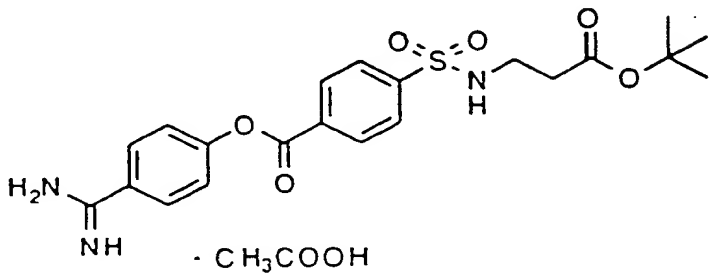
N-[[3-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-glutamic acid di-t-butyl ester



TLC : Rf 0.59 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD): δ 8.44 (1H, t, J=2.0Hz), 8.22 (1H, dt, J=8.0Hz, 2.0Hz), 8.08 (1H, dt, J=8.0Hz, 2.0Hz), 8.06 (2H, d, J=9.0Hz), 7.87 (2H, d, J=9.0Hz), 7.74 (1H, t, J=8.0Hz), 3.92 (1H, dd, J=9.0Hz, 5.0Hz), 2.37 (2H, m), 1.98 (1H, m), 1.76 (1H, m), 1.45 (9H, s), 1.25 (9H, s).

Example 9(10)

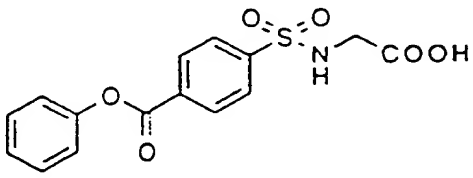
N-[[4-[(4-Amidinophenoxy)carbonyl]phenyl]sulfonyl]-β-alanine t-butyl ester acetate



TLC : Rf 0.35 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD): δ 8.40 (2H, d, J=8.0Hz), 8.05 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 7.60 (2H, d, J=8.0Hz), 3.15 (2H, t, J=6.0Hz), 2.45 (2H, t, J=6.0Hz), 2.00 (3H, s), 1.45 (9H, s).

Example 10

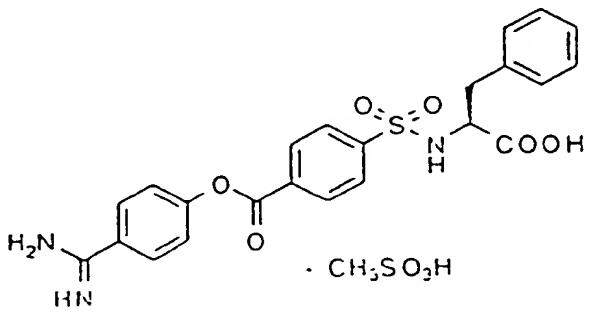
N-[[4-(Phenoxycarbonyl)phenyl]sulfonyl]glycine



The title compound having the following physical data was obtained by the same procedure as a series of reactions of Example 2. using a compound prepared in Example 9 instead of a compound prepared in Example 1.
TLC: Rf 0.22 (Chloroform : Ethyl acetate : Acetic acid : Water = 90 : 10 : 1 : 1),
NMR ($CDCl_3$+CD_3OD): δ 8.33 (2H, d. J=8.8Hz), 8.02 (2H, d, J=8.8Hz), 7.46 (2H, t, J=7.4Hz), 7.33 (1H, t, J=7.4Hz), 7.21 (2H. d. J=7.4Hz), 3.81 (2H. s).

Example 10(1)-10(12)

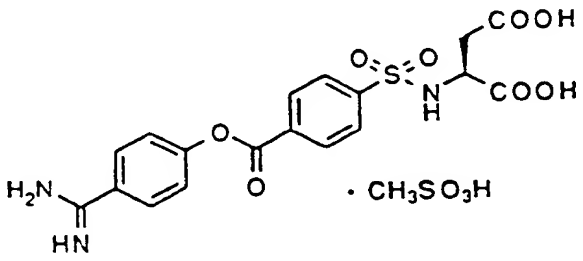
The compounds having the following physical data were obtained by the same procedure as a series of reactions of Example 10. if necessary, by converting to corresponding salts by conventional method, using a compound prepared in Example 7. 8 and 9(1)-9(10). N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-L-phenylalanine methansulfonate



TLC : Rf 0.74 (Chloroform : Methanol : Acetic acid = 3 : 1 : 1),
NMR (CD_3OD): δ 8.20 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 7.80 (2H, d, J=8.0Hz), 7.60 (2H, d, J=8.0Hz), 7.25-7.10 (5H, m), 4.10 (1H, dd, J=9.0, 5.0Hz), 3.10 (1H, dd, J=14, 5.0Hz), 2.85 (1H, dd, J=14, 9.0Hz), 2.70 (3H, s).

Example 10(2)

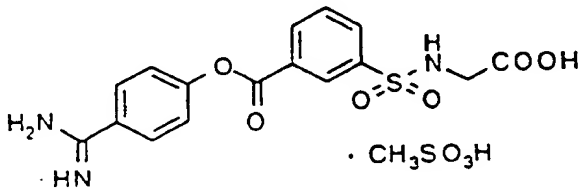
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-L-aspartic acid methansulfonate



TLC : Rf 0.21 (Chloroform : Methanol : Acetic acid = 3 : 1 : 1),
NMR (CD_3OD):δ 8.35 (2H, d, J=8.0Hz), 8.10 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 7.55 (2H, d, J=8.0Hz), 4.30 (1H, t, J=6.5Hz), 2.80 (2H, d, J=6.5Hz), 2.70 (3H, s).

Example 10(3)

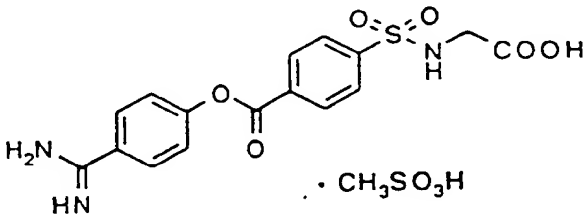
N-[[3-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]glycine methansulfonate



TLC : Rf 0.27 (Chloroform : Methanol : Acetic acid = 3 : 1 : 1),
NMR (CD_3OD):δ 8.85 (1H, br.s), 8.40 (1H, d, J=8.0Hz), 8.20 (1H, d, J=8.0Hz), 7.95 (2H, d, J=9.0Hz), 7.80 (1H, t, J=8.0Hz), 7.60 (2H, d, J=9.0Hz), 3.80 (2H, s), 2.70 (3H, s).

Example 10(4)

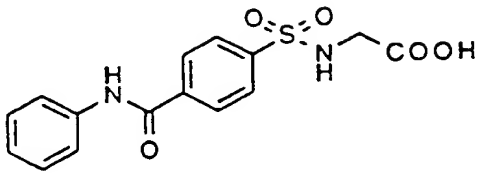
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]glycine methansulfonate



TLC : Rf 0.30 (Chloroform : Methanol : Acetic acid = 3 : 1 : 1),
NMR (CD_3OD):δ 8.35 (2H, d, J=8.0Hz), 8.05 (2H, d, J=8.0Hz), 7.95 (2H, d, J=9.0Hz), 7.60 (2H, d, J=9.0Hz), 3.80 (2H, s), 2.70 (3H, s).

Example 10(5)

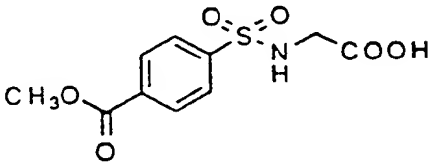
N-[[4-(N-Phenylcarbamoyl)phenyl]sulfonyl]glycine



TLC : Rf 0.04 (Chloroform : Methanol : Acetic acid : Water = 100 : 10 : 1 : 1),
NMR ($CDCl_3$+CD_3OD+DMSO-d6): δ 8.10 (2H, d, J=8.3Hz), 7.95 (2H, d, J=8.3Hz), 7.75 (2H, d, J=8.0Hz), 7.35 (2H, t, J=8.0Hz), 7.13 (1H, t, J=8.0Hz), 3.67 (2H, s).

Example 10(6)

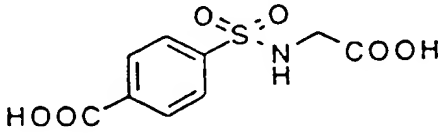
N-[(4-Methoxycarbonylphenyl)sulfonyl]glycine



TLC : Rf 0.16 (Chloroform : Methanol : Acetic acid : Water = 90 : 10 : 1 : 1),
NMR ($CDCl_3$+CD_3OD): δ 8.13 (2H, d, J=8.8Hz), 7.90 (2H, d, J=8.8Hz), 3.92 (3H, s), 3.74 (2H, s).

Example 10(7)

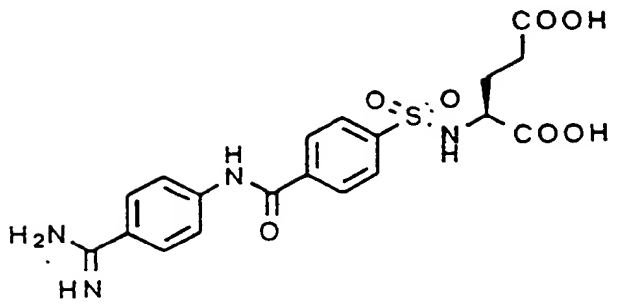
N-[(4-Carboxyphenyl)sulfonyl]glycine



TLC : Rf 0.02 (Chloroform : Methanol : Acetic acid : Water = 90 : 10 : 1 : 1),
NMR (DMSO-d6):δ 8.25 (1H, t, J=6.2Hz), 8.08 (2H, d, J=8.8Hz), 7.89 (2H, d, J=8.8Hz), 3.63 (2H, d, J=6.2Hz).

Example 10(8)

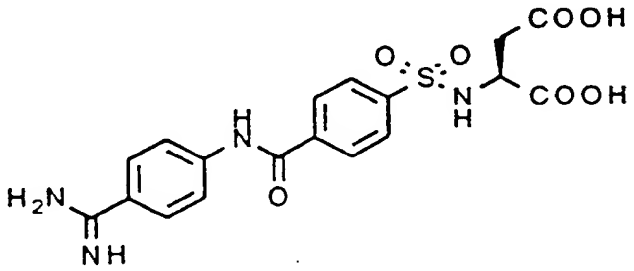
N-[[4-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-glutamic acid



TLC : Rf 0.51 (Ethyl acetate : Acetic acid : Water = 3 : 1 : 1),
NMR (DMSO-d6+ $MeSO_3H$(1drop)): δ 10.85 (1H, s), 9.24 (2H, s), 8.98 (2H, s), 8.39 (1H, d, J=9.0Hz), 8.15 (2H, d, J=9.0Hz), 8.03 (2H, d, J=9.0Hz), 7.93 (2H, d, J=9.0Hz), 7.87 (2H, d, J=9.0Hz), 3.85 (1H, dt, J=9.0Hz, 7Hz), 2.23 (2H, t, J=7.0Hz), 2.00-1.60 (2H, m).

Example 10(9)

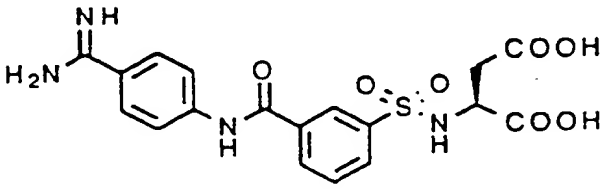
N-[[4-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-aspartic acid



TLC : Rf 0.51 (Ethyl acetate : Acetic acid : Water = 3 : 1 : 1),
NMR (DMSO-d6+ $MeSO_3H$(1drop)):δ 10.85 (1H, s), 9.24 (2H, s), 8.97 (2H, s), 8.43 (1H, d, J=9.0Hz), 8.14 (2H, d, J=9.0Hz), 8.03 (2H, d, J=9.0Hz), 7.95 (2H, d, J=9.0Hz), 7.87 (2H, d, J=9.0Hz), 4.13 (1H, dt, J=9.0Hz, 6.0Hz), 2.64 (1H, dd, J=16.0Hz, 6.0Hz), 2.46 (1H, dd, J=16.0Hz, 6.0Hz).

Example 10(10)

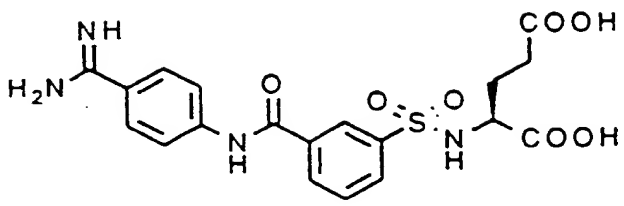
N-[[3-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-aspartic acid



TLC : Rf 0.67 (Ethyl acetate : Acetic acid : Water = 3 : 1 : 1),
NMR (DMSO-d6+ $MeSO_3H$(1drop)): δ 10.88 (1H, s), 9.24 (2H, s), 8.95 (2H, s), 8.40 (1H, s), 8.23 (1H, d, J=8.0Hz), 8.03 (2H, d, J=9.0Hz), 8.02 (1H, d, J=8.0Hz), 7.87 (2H, d, J=9.0Hz), 7.76 (1H, t, J=8.0Hz), 4.14 (1H, m), 2.64 (1H, dd, J=16Hz, 6.0Hz), 2.46 (1H, dd, J=16Hz, 6.0Hz).

Example 10(11)

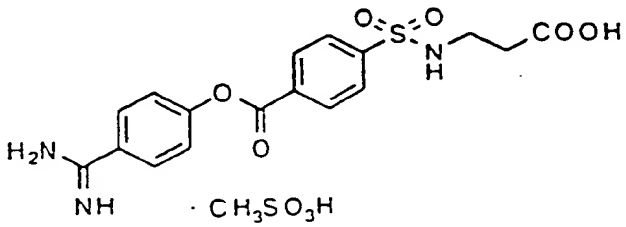
N-[[3-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-glutamic acid



TLC : Rf 0.65 (Ethyl acetate : Acetic acid : Water = 3 : 1 : 1),
NMR (DMSO-d6+ $MeSO_3H$(1drop)):δ 10.88 (1H, s), 9.24 (2H, s), 9.01 (2H, s), 8.37 (1H, s), 8.35 (1H, d, J=8.0Hz), 8.24 (1H, d, J=8.0Hz), 8.03 (2H, d, J=9.0Hz), 8.01 (1H, d, J=8.0Hz), 7.87 (2H, d, J=9.0Hz), 7.76 (1H, t, J=8.0Hz), 3.85 (1H, m), 2.22 (2H, t, J=7.0Hz), 1.90 (1H, m), 1.69 (1H, m).

Example 10(12)

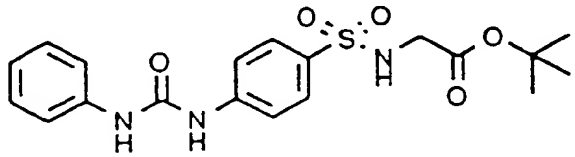
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-β-alanine methansulfonate



TLC : Rf 0.34 (Chloroform : Methanol : Acetic acid = 10 : 2 : 1),
NMR (CD_3OD): δ 8.40 (2H, d, J=8.0Hz), 8.05 (2H, d, J=8.0Hz), 7.95 (2H, d, J=8.0Hz), 7.60 (2H, d, J=8.0Hz), 3.20 (2H, t, J=6.5Hz), 2.75 (3H, s), 2.55 (2H, t, J=6.5Hz).

Example 11

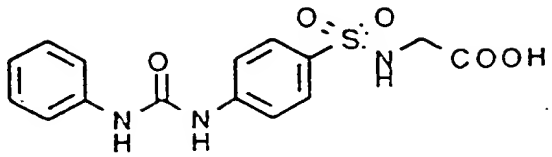
N-[[4-(N-Phenylureido)phenyl]sulfonyl]glycine t-butyl ester



To a solution of a compound prepared in reference example 2 (1.20 g) in acetone (20 ml), phenyl isocyanate (500 µl) was added. After the mixture was stirred for 24 hours at room temperature, phenyl isocyanate (200µl) was added to the mixture. The mixture was stirred for 24 hours. Additional phenyl isocyanate (500µl) was added and the mixture was stirred for 12 hours. The reaction mixture was concentrated. The residue was washed with ether and dried to give the title compound (1.40 g) having the following physical data.
TLC: Rf 0.25 (Hexane : Ethyl acetate = 1 : 1),
NMR ($CDCl_3$): δ 7.72-7.60 (1H), 7.66 (2H, d, J=8.8Hz), 7.46-7.20 (5H, m), 7.28 (2H, d, J=8.8Hz), 7.12-7.00 (1H, m), 5.39 (1H, t, J=5.6Hz), 3.63 (2H, d, J=5.6Hz), 1.36 (9H, s).

Example 12

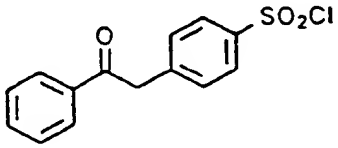
N-[[4-(N-Phenylureido)phenyl]sulfonyl]glycine



The title compound having the following physical data was obtained by the same procedure as a series of reactions of Example 2, using a compound prepared in Example 11.
TLC : Rf 0.34 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 9.08 (1H, s), 8.77 (1H, s), 7.82 (1H, t, J=6.2Hz), 7.69 (2H, d, J=9.0Hz), 7.60 (2H, d, J=9.0Hz), 7.52-7.40 (2H, m), 7.28 (2H, t, J=7.4Hz), 6.98 (1H, t, J=7.4Hz), 3.53 (2H, d, J=6.2Hz)

Reference example 8

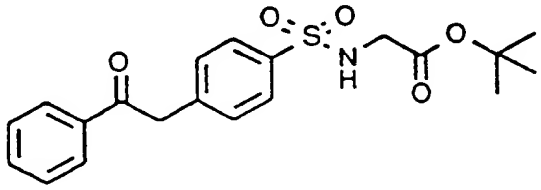
2-(4-Chlorosulfonyl)phenylacetophenone



Deoxybenzoine (5.0 g) was added by portions to sulfonyl chloride (8.45 ml) at 0°C. The solution was stirred for 30 minutes at 10-15°C and then stirred for 15 minutes at 50°C. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The extract was washed with water, a saturated aqueous solution of sodium chloride, dried over anhydrous magnesium sulfate and concentrated. The residue was washed with ether and dried to give the title compound (2.25 g). Besides, the ether layer was purified by column chromatography on silica gel (hexane : ethyl acetate = 17 : 3) to give additional title compound (1.09g: total 3.34 g) having the following physical data.
TLC: Rf 0.27 (Hexane : Ethyl acetate = 9 : 1).

Example 13

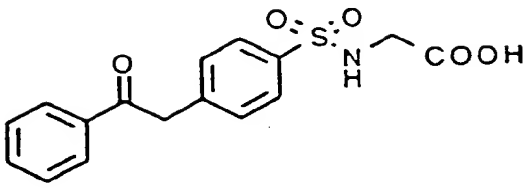
N-[(4-Benzoylmethylphenyl)sulfonyl]glycine t-butyl ester



The title compound having the following physical data was obtained by the same procedure as a series of reactions of Example 4, using a compound prepared in reference Example 8.
TLC : Rf 0.21 (Hexane : Ethyl acetate = 7 : 3),
NMR ($CDCl_3$): δ 8.05-7.97 (2H, m), 7.83 (2H, d, J=8.6Hz), 7.65-7.45 (3H, m), 7.41 (2H, d, J=8.6Hz), 5.05 (1H, t, J=5.4Hz), 4.35 (2H, s), 3.67 (2H, d, J=5.4Hz), 1.34 (9H, s).

Example 14

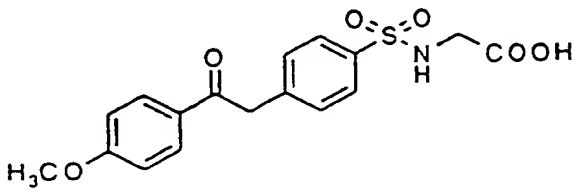
N-[(4-Benzoylmethylphenyl)sulfonyl]glycine



The title compound having the following physical data was obtained by the same procedure as a series of reactions of Example 3, using a compound prepared in Example 13.
TLC : Rf 0.56 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.50-11.50 (1H, br.s), 8.10-8.00 (2H, m), 7.98 (1H, t, J=6.2Hz), 7.74 (2H, d, J=8.4Hz), 7.72-7.50 (3H, m), 7.45 (2H, d, J=8.4Hz), 4.53 (2H, s), 3.57 (2H, d, J=6.2Hz).

Example 14(1)

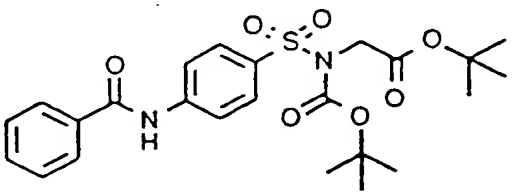
N-[4-[(4-Methoxybenzoyl)methyl]sulfonyl]glycine



The title compound having the following physical data was obtained by the same procedure as a series of reactions of Example 3, using N-[4-[(4-Methoxybenzoyl)methyl]sulfonyl]glycine t-butyl ester which was obtained by the same procedure as a series of reactions of reference Example 8 and Example 14 using corresponding compounds.
TLC : Rf 0.35 (Chloroform : Methanol : Acetic acid : Water = 50 : 10 : 1 : 1),
NMR ($CDCl_3$+CD_3OD): δ 8.00 (2H, d, J=8.8Hz), 7.82 (2H, d, J=8.3Hz), 7.41 (2H, d, J=8.3Hz), 6.98 (2H, d, J=8.8Hz), 4.36 (2H, s), 3.90 (3H, s), 3.71 (2H, s).

Reference example 9

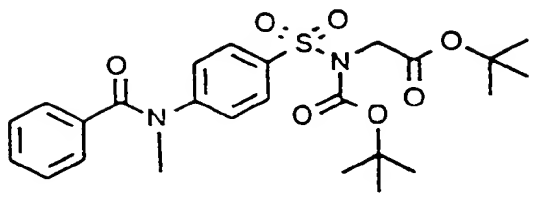
N-[[4-(Benzoylamino)phenyl]sulfonyl]-N-t-butoxycarbonylglycine t-butyl ester



To a solution of a compound prepared in example 1(10) (1.20 g) in acetonitrile (60 ml), 4-dimethylaminopyridine (37 mg) and di-t-butyl dicarbonate (811 µl) were added. The mixture was stirred for 30 minutes at room temperature. The reaction mixture was concentrated and extracted with ethyl acetate. The extract was washed with water, a saturated aqueous solution of sodium bicarbonate, water and a saturated aqueous solution of sodium chloride, successively, dried over anhydrous magnesium sulfate and concentrated to give the title compound (1.61 g) having the following physical data.
TLC: Rf 0.61 (Hexane : Ethyl acetate = 1 : 1).

Reference example 10

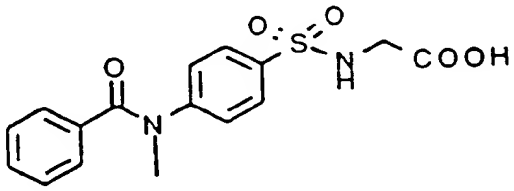
N-[[4-(N-Methyl-N-benzoylamino)phenyl]sulfonyl]-N-t-butoxycarbonylglycine t-butyl ester



To a solution of a compound prepared in reference example 9 (1.60 g) in dimethylformamide (20 ml), 60% sodium hydride (143 mg) was added at 0°C. The mixture was stirred for 1 hour. To the reaction mixture, Iodomethane (558 µl) was added. The mixture was stirred for 30 minutes. Water was added to the reaction mixture, and then the mixture was extracted with ethyl acetate. The extract was washed a saturated aqueous solution of sodium chloride, dried over anhydrous magnesium sulfate and concentrated. The residue was purified by column chromatography on silica gel (hexane : ethyl acetate = 7 : 3) to give the title compound (1.05 g) having the following physical data.
TLC: Rf 0.54 (Hexane : Ethyl acetate = 1 : 1).

Example 15

N-[[4-(N-Methyl-N-benzoylamino)phenyl]sulfonyl]glycine



The title compound (641 mg) having the following physical data was obtained by the same procedure as Example 2, using a compound prepared in reference example 10 (1.00 g).
TLC : Rf 0.47 (Chloroform : Methanol : Acetic acid = 16 : 3 : 1),
NMR (DMSO-d6): δ 13.20-12.00 (1H, br.s), 8.00 (1H, t, J=5.8Hz), 7.65 (2H, d, J=8.8Hz), 7.33 (2H, d, J=8.8Hz), 7.31-7.20 (5H, m), 3.51 (2H, d, J=5.8Hz), 3.40 (3H, s).

Formulation example 1

The following components were admixed in conventional method and punched out to obtain 100 tablets each containing 50 mg of active ingredient.

- N-[[4-(p-Toluoylamino)phenyl]sulfonyl]glycine 5g
- Carboxymethyl Cellulose calcium (disintegrating agent) 0.2g
- Magnesium stearate (lubricating agent) 0.1g
- Microcrystalline cellulose 4.7g

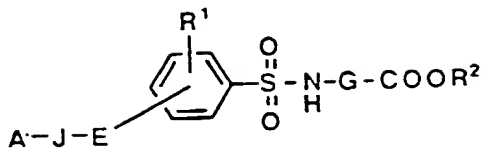
Formulation example 2

The following components were admixed in conventional method. The solution was sterilized in conventional manner, placed 2 ml portions into 5 ml ampoules and freeze-dried to obtain 100 ampoules each containing 20 mg of the active ingredient.

- N-[[4-(p-Toluoylamino)phenyl]sulfonyl]glycine 2.00g
- mannitol 20 g
- distilled water 500 ml

Claims

1. Use of a compound of formula (Ia) :



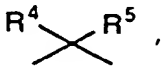
(Ia)

wherein

R^1 is hydrogen, or C1-4 alkyl;
R^2 is (1) hydrogen, (2) C1-8 alkyl, (3) phenyl, or (4) C1-4 alkyl substituted by phenyl, $-OCOR^{16}$, in which R^{16} is C1-4 alkyl; or $-CONR^{17}R^{18}$, in which R^{17} and R^{18} each, independently, is hydrogen or C1-4 alkyl;
E is

(1) $-CONR^3-$, in which R^3 is hydrogen, C1-4 alkyl, phenyl, or C1-4 alkyl substituted by phenyl;
(2) $-NR^3CO-$, in which R^3 is as hereinbefore defined;
(3) -CO-O-,
(4) -O-CO-,
(5) $-NR^3-CO-NR^3-$, in which R^3 is as hereinbefore defined;
(6) $-CO-CH_2-$,
(7) -CO-,
(8) $-O-CO-NR^3-$, in which R^3 is as hereinbefore defined;
(9) $-NR^3-CO-O-$, in which R^3 is as hereinbefore defined;
(10) -O-CO-O-,
(11) $-CS-NR^3-$, in which R^3 is as hereinbefore defined;
(12) $-NR^3-CS-$, in which R^3 is as hereinbefore defined;
(13) $-NR^3-CS-NR^3-$, in which R^3 is as hereinbefore defined;
(14) $-O-CS-NR^3-$, in which R^3 is as hereinbefore defined;
(15) $-NR^3-CS-O-$, in which R^3 is as hereinbefore defined;
(16) -CS-O-,
(17) -O-CS-, or
(18) -O-CS-O-.

A is (1) hydrogen, (2) C1-8 alkyl, (3) C3-7 cycloalkyl, or (4) Ar, in which Ar is carbocyclic aryl or heterocyclic aryl, and is unsubstituted or substituted by 1-3 of C1-15 alkyl, C1-15 alkoxy, halogen, nitro, cyano, guanidino, amidino, hydroxy, benzyloxy, $-NR^9R^{10}$, in which R^9 and R^{10} each, independently, is hydrogen or C1-4 alkyl; $-COOR^{11}$, in which R^{11} is hydrogen or C1-4 alkyl; trifluoromethyl, phenyl or heterocyclic ring;
J is (1) a bond, (2) C2-4 alkylene, (3) C2-4 alkenylene, or (4)



in which R^4 and R^5 each, independently, is (i) hydrogen, (ii) C1-4 alkyl, or (iii) C1-4 alkoxy, or R^4 and R^5, taken together with the carbon to which they are attached, form a C3-7 cycloalkyl group,
G is (1) $-(CH_2)_m-$, in which m is 2, 3 or 4, or (2)

in which R^6 and R^7 each, independently, is (i) hydrogen, (ii) C1-8 alkyl, (iii) $-COOR^8$, in which R^8 is hydrogen,

C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl; (iv) Ar, in which Ar is as hereinbefore defined; (v) heterocyclic ring, (vi) C1-8 alkyl substituted by: -$COOR^8$, in which R^8 is as hereinbefore defined; C1-4 alkoxy; hydroxy; benzyloxy; -$NR^{12}R^{13}$, in which R^{12} and R^{13} each, independently, is hydrogen or C1-4 alkyl; -$NR^{14}COOR^{15}$, in which R^{14} is hydrogen or C1-4 alkyl, and R^{15} is hydrogen, C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl; Ar; or heterocyclic ring; with the proviso that one of the carbon atoms in C1-8 alkyl may be . replaced by a sulfur atom; or R^6 and R^7, taken together with the carbon to which they are attached, form a C3-7 cycloalkyl group;

with the proviso that, when E is -O-CO-NR^3-, -O-CO-O-, -O-CS-NR^3- or -O-CS-O-, and J is a bond, A is not hydrogen;

or a non-toxic salt thereof, in the manufacture of a medicament for the prevention and/or treatment of a disease induced by overexpression or excess activity of a metalloproteinase.

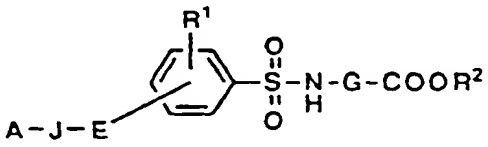
2. Use according to claim 1, in which the disease induced by overexpression or excess activity of a matrix metalloproteinase is a rheumatoid disease, arthrosteitis, unusual bone resorption, osteoporosis, periodontitis, interstitial nephritis, arteriosclerosis, pulmonary emphysema, cirrhosis, cornea injury, metastasis, invasion or growth of tumor cells, an autoimmune disease, a disease caused by vascular emigration or infiltration of leukocytes, or arterialization.

3. Use according to claim 1 or 2, wherein the compound of formula (Ia) is selected from

N-[[4-(Benzoylamino)phenyl]sulfonyl]glycine,
N-[[3-(Benzoylamino)phenyl]sulfonyl]glycine,
N-[[2-(Benzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Acetylamino)phenyl]sulfonyl]glycine,
N-[[4-(Phenylacetylamino)phenyl]sulfonyl]glycine,
N-[[4-[(Phenylethylcarbonyl)amino]phenyl]sulfonyl]glycine,
N-[[4-(Cinnamoylamino)phenyl]sulfonyl]glycine,
N-[[4-(N-Phenylureido)phenyl]sulfonyl]glycine,
N-[[4-(N-Phenylthioureido)phenyl]sulfonyl]glycine,
N-[[4-[(Benzyloxycarbonyl)amino]phenyl]sulfonyl]glycine,
N-[[4-[(Phenyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine,
N-[[4-[(Benzyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine,
N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Formylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-D-α-phenyl glycine,
N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-L-α-phenyl glycine,
N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-D-α-phenyl glycine,
N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-L-α-phenyl glycine,
N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-D-α-phenyl glycine,
N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-L-α-phenyl glycine,
N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-D-α-phenyl glycine,
N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-α-phenyl glycine,
N-[(4-Pivaloyloxyphenyl)sulfonyl]-D,L-α-phenylglycine,
N-[(4-Pivaloyloxyphenyl)sulfonyl]-D,L-phenylalanine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-alanine,
N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-β-alanine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine,
N-[[4-(2.4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-valine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-leucine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-serine,

N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-phenylalanine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D,L-alanine methyl ester,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine methyl ester,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-valine methyl ester,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine methyl ester,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-serine methyl ester,
N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine methyl ester,
N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
N-[[3-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
N-[[4-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
N-[[3-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-glutamic acid,
N-[[4-(4-chlorobenzoylamino)phenyl]sulfonyl]-L-glutamic acid,
N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-glutamic acid,
N-[[4-[2-(4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
N-[[4-[2-(4-(1-Nitrophenyl)butyryloxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
N-[[4-(2-Methoxy-2-phenylacetyloxy)phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
N-[[4-[1-(4-Nitrophenyl)cyclobutyl]carbonyl]oxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-t-butoxycarbonyl-L-lysine,
N-[[4-(2-Phenylbutyryloxy)phenyl]sulfonyl]glycine,
N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-phenylalanine,
N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-aspartic acid,
N-[[4-[[[1-(4-Nitrophenyl)cyclobutyl]carbonyl]oxy]phenyl]sulfonyl]-D,L-aspartic acid,
1-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonylamide]-1-cyclopropanecarboxylic acid,
N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-furanyl)glycine,
N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-thienyl)glycine,
N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-valine,
N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-S-carboxymethyl-L-cysteine,
N-[[4-[2-Ethyl-2-(4-methoxyphenyl)butyryloxy]phenyl]sulfonyl]-glycine,
N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-lysine,
5-[N-[[3-Methyl-4-[2-[4-(1-pyrrolidinyl)phenyl]butylyloxy]phenyl]sulfonyl]amino]pentanoic acid, and
N-[[(3-Methyl-4-pivaloyloxy)phenyl]sulfonyl]-β-alanine.

4. A compound of the formula (Ib):



(Ib)

wherein

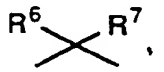
R^1 is hydrogen, or C1-4 alkyl;
R^2 is (1) hydrogen, (2) C1-8 alkyl, (3) phenyl, or (4) C1-4 alkyl substituted by phenyl, $-OCOR^{16}$, in which R^{16} is C1-4 alkyl; or $-CONR^{17}R^{18}$, in which R^{17} and R^{18} each, independently, is hydrogen or C1-4 alkyl;
E is

(1) $-CONR^3-$, in which R^3 is hydrogen, C1-4 alkyl, phenyl, or C1-4 alkyl substituted by phenyl;
(2) $-NR^3CO-$, in which R^3 is as hereinbefore defined;
(3) -CO-O-,
(4) -O-CO-,
(5) $-NR^3-CO-NR^3-$, in which R^3 is as hereinbefore defined;
(6) $-CO-CH_2-$,
(7) -CO-,
(8) $-O-CO-NR^3-$, in which R^3 is as hereinbefore defined;

(9) -NR^3-CO-O-, in which R^3 is as hereinbefore defined;
(10) -O-CO-O-,
(11) -CS-NR^3-, in which R^3 is as hereinbefore defined;
(12) -NR^3-CS-, in which R^3 is as hereinbefore defined;
(13) -NR^3-CS-NR^3-, in which R^3 is as hereinbefore defined;
(14) -O-CS-NR^3-, in which R^3 is as hereinbefore defined;
(15) -NR^3-CS-O-, in which R^3 is as hereinbefore defined;
(16) -CS-O-,
(17) -O-CS-,
(18) -O-CS-O-, or

A is is (1) hydrogen, (2) C1-8 alkyl, (3) C3-7 cycloalkyl, or (4) Ar, in which Ar is carbocyclic aryl or heterocyclic aryl, and is unsubstituted or substituted by 1-3 of C1-15 alkyl, C1-15 alkoxy, halogen, nitro, cyano, guanidino, amidino, hydroxy, benzyloxy, -NR^9R^{10}, in which R^9 and R^{10} each, independently, is hydrogen or C1-4 alkyl; -$COOR^{11}$, in which R^{11} is hydrogen or C1-4 alkyl; trifluoromethyl, phenyl or heterocyclic ring;
J is (1) a bond, (2) C2-4 alkylene, (3) C2-4 alkenylene, or (4)

in which R^4 and R^5 each, independently, is (i) hydrogen, (ii) C1-4 alkyl, or (iii) C1-4 alkoxy, or R^4 and R^5, taken together with the carbon to which they are attached,
form a C3-7 cycloalkyl group,
G is (1) -$(CH_2)_m$-, in which m is 2, 3 or 4, or (2)



in which R^6 and R^7 each, independently, is (i) hydrogen, (ii) C1-8 alkyl, (iii) -$COOR^8$, in which R^8 is hydrogen, C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl; (iv) Ar, in which Ar is as hereinbefore defined; (v) heterocyclic ring, (vi) C1-8 alkyl substituted by: -$COOR^8$, in which R^8 is as hereinbefore defined; C1-4 alkoxy; hydroxy; benzyloxy; -$NR^{12}R^{13}$, in which R^{12} and R^{13} each, independently, is hydrogen or C1-4 alkyl; -$NR^{14}COOR^{15}$, in which R^{14} is hydrogen or C1-4 alkyl, and R^{15} is hydrogen, C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl; Ar; or heterocyclic ring; with the proviso that one of the carbon atoms in C1-8 alkyl may be replaced by a sulfur atom; or R^6 and R^7, taken together with the carbon to which they are attached, form a C3-7 cycloalkyl group;
with the proviso that, when E is -O-CO-NR^3-, -O-CO-O-, -O-CS-NR^3- or -O-CS-O-, and J is a bond, A is not hydrogen;
or a non-toxic salt thereof;
with the exclusion of the following compounds:

(1) N-[[4-(Benzoylamino)phenyl]sulfonyl]glycine,
(2) N-[[3-(Benzoylamino)phenyl]sulfonyl]glycine,
(3) N-[[2-(Benzoylamino)phenyl]sulfonyl]glycine,
(4) N-[[4-(Acetylamino)phenyl]sulfonyl]glycine,
(5) N-[[4-(Phenylacetylamino)phenyl]sulfonyl]glycine,
(6) N-[[4-[(Phenylethylcarbonyl)amino]phenyl]sulfonyl]glycine,
(7) N-[[4-(Cinnamoylamino)phenyl]sulfonyl]glycine,
(8) N-[[4-(N-Phenylureido)phenyl]sulfonyl]glycine,
(9) N-[[4-(N-Phenylthioureido)amino]phenyl]sulfonyl]glycine,
(10) N-[[4-[(Benzyloxycarbonyl)amino]phenyl]sulfonyl]glycine,
(11) N-[[4-[(Phenyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine,
(12) N-[[4-[(Benzyloxymethylcarbonyl)amino]phenyl]sulfonyl]glycine,
(13) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]glycine,
(14) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]glycine,

(15) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(16) N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(17) N-[[4-(2-Nitrobenzoylamino)phenyl]sulfonyl]glycine,
(18) N-[[4-(4-Formylbenzoylamino)phenyl]sulfonyl]glycine,
(19) N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(20)N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(21) N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-D-α-phenylglycine,
(22) N-[[4-(4-Methylbenzoylamino)phenyl]sulfonyl]-L-α-phenylglycine,
(23) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-D-α-phenyl-glycine,
(24) N-[[4-(4-Methoxybenzoylamino)phenyl]sulfonyl]-L-α-phenyl-glycine,
(25) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-D-α-phenyl-glycine,
(26) N-[[4-(4-Fluorobenzoylamino)phenyl]sulfonyl]-L-α-phenyl-glycine,
(27) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-D-α-phenyl-glycine,
(28) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-α-phenyl-glycine,
(29) N-[(4-Pivaloyloxyphenyl)sulfonyl]-D,L-α-phenyl-glycine,
(30) N-[(4-Pivaloyloxyphenyl)sulfonyl]-D,L-phenylalanine,
(31) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]glycine,
(32) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-alanine,
(33) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-β-alanine,
(34) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine,
(35) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-valine,
(36) N- [[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine,
(37) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-leucine,
(38) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-serine,
(39) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-phenylalanine,
(40) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine,
(41) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-alanine methyl ester,
(42) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-valine methyl ester,
(43) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-valine methyl ester,
(44) N-[[4-[[(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-leucine methyl ester,
(45) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-D, L-serine methyl ester,
(46) N-[[4-(2,4-Dichlorobenzoylamino)phenyl]sulfonyl]-L-tyrosine methyl ester,
(47) N-[[4-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
(48) N-[[3-(3-Nitrobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
(49) N-[[4-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
(50) N-[[3-(3-Aminobenzoylamino)phenyl]sulfonyl]-L-aspartic acid,
(51) N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-glutamic acid,
(52) N-[[4-(4-chlorobenzoylamino)phenyl]sulfonyl]-L-glutamic acid,
(53) N-[[4-(4-Nitrobenzoylamino)phenyl]sulfonyl]-L-glutamic acid,
(54) N-[[4-[2-(4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
(55) N-[[4-[2-(4-(1-Nitrophenyl)butyryloxy]phenyl]sulfonyl]-D,L-3-morpholino alanine ethyl ester,
(56) N-[[4-(2-Methoxy-2-phenylacetyloxy)phenyl]sulfonyl]-D,L-3-morpholino alanine ethyl ester,
(57) N-[[4-[[[1-(4-Nitrophenyl)cyclobutyl]carbonyl]oxy]phenyl]sulfonyl]-D,L-3-morpholinoalanine ethyl ester,
(58) N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-t-butoxycarbonyl-L-lysine,
(59) N-[[4-(2-Phenylbutyryloxy)phenyl]sulfonyl]glycine,
(60) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-phenyl alanine,
(61) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-aspartic acid,
(62) N-[[4-[[[1-(4-Nitrophenyl)cyclobutyl]carbonyl]oxy]phenyl]sulfonyl]-D, L-aspartic acid,
(63) 1-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonylamide]-1-cyclopropanecarboxylic acid,
(64) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-furanyl)glycine,
(65) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-D,L-2-(2-thienyl)glycine,
(66) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-valine,
(67) N-[[4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-S-carboxymethyl-L-cysteine,
(68) N-[[4-[2-Ethyl-2-(4-methoxyphenyl)butyryloxy]phenyl]sulfonyl]-glycine,
(69) N-[[3-Methyl-4-[2-[4-(1-Pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]-L-lysine,
(70) 5-[N-[[3-Methyl-4-[2-[4-(1-pyrrolidinyl)phenyl]butyryloxy]phenyl]sulfonyl]amino]pentanoic acid, and
(71) N-[[(3-Methyl-4-pivaloyloxy)phenyl]sulfonyl]-β-alanine.

5. A compound according to claim 4, wherein E is -CONR^3-, -NR^{3}CO-, -NR^3-CO-NR^3-, -O-CO-NR^3-, -NR-CO-O-, -CS-NR^3-, -NR^3-CS-, -NR^3-CS-NR^3-, -O-CS-NR^3- or -NR^3-CS-O-.

6. A compound according to claim 4, wherein E is -CO-O-, -O-CO-, -CO-CH$_2$-, -CO-, -O-CO-O-, -CS-O-, -O-CS- or -O-CS-O-.

7. A compound according to claim 4, which is selected from

N-[[4-(p-Toluoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Isobutyrylamino)phenyl]sulfonyl]glycine,
N-[[4-(Acetylamino)phenyl]sulfonyl]glycine,
N-[[4-(o-Toluoylamino)phenyl]sulfonyl]glycine,
N-[[4-(m-Toluoylamino)sulfonyl]glycine,
N-[[4-(2-Chlorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Chlorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Chlorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Methoxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Methoxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Ethylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Propylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Fluorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Fluorobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Cyclohexylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Trifluoromethylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Thienylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Furylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Pyridylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Pyridylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Pyridylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Thienylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Furylcarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Methoxycarbonylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Cyanobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Carboxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-[(4-Butylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Pentylbenzoylamino)phenyl]sulfonyl]glycine,
N- [[4-(4-Phenylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-valine,
N-[[4-(1-Naphthoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Naphthoylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Benzyloxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-aspartic acid,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-leucine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-leucine,
N-[[4-(Phenoxycarbonylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Dimethylaminobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-valine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-Phenylalanine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-Phenylalanine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-alanine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-alanine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-lysine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-lysine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-glutamic acid,
N-[[4-(4-Dodecylbenzoylamino)phenyl]sulfonyl]glycine,
4-[N-[[4-(Benzoylamino)phenyl]sulfonyl]amino]butyric acid,

N-[[4-(Benzoylamino)phenyl]sulfonyl]amino}-L-serine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]amino}-D-serine,
N-[[4-(Benzoylamino)phenyl]sulfonyl}-D-aspartic acid,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl}-D-phenylalanine,
N-[[4-(4-Pentylbenzoylamino)phenyl]sulfonyl]-D-phenylalanine,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl}-L-valine,
N-[[4-(4-Hexylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Heptylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Isopropylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Isobutylbenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-2,2-dimethylglycine,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]amino}-D-serine,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-L-leucine,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-alanine,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-valine,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-leucine,
N-[[2-Methyl-4-(p-Toluoylamino)phenyl]sulfonyl]glycine,
N-[[3-Methyl-4-(p-Toluoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Hydroxy-4-methylbenzoylamino)phenyl]sulfonyl]-D-alanine,
N-[[4-(2-Thienylcarbonylamino)phenyl]sulfonyl]-D-alanine,
N-[[3-(Benzoylamino)phenyl]sulfonyl]glycine,
N-[[2-(Benzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Aminobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(3-Aminobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Aminobenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(4-Hydroxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-[(2-Phenylethyl)carbonylamino]phenyl]sulfonyl]glycine,
N-[[4-(3-Hydroxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(2-Hydroxybenzoylamino)phenyl]sulfonyl]glycine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-tryptophan,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-L-tyrosine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-tryptophan,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-tyrosine,
N-[[4-(Benzoylamino)phenyl]sulfonyl]-D-histidine,
2-[N-[4-(Benzoylamino)phenyl]sulfonylamino]-(3-pyridyl)-D-alanine,
N-[[4-(p-Toluoylamino)phenyl]sulfonyl]-D-tryptophan,
N-[[4-(N-Phenylcarbamoyl)phenyl]sulfonyl]glycine,
N-[[4-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-glutamic acid,
N-[[4-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-aspartic acid,
N-[[3-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-aspartic acid,
N-[[3-[N-(4-Amidinophenyl)carbamoyl]phenyl]sulfonyl]-L-glutamic acid, and
N-[[4-(N-Methyl-N-benzoylamino)phenyl]sulfonyl]glycine,

and esters and non-toxic salts thereof.

8. A compound according to claim 4, which is selected from

N-[[4-(Benzyloxycarbonyloxy)phenyl]sulfonyl]glycine,
N-[[4-(Benzoyloxy)phenyl]sulfonyl]glycine,
N-[[4-(4-Amidinobenzoyloxy)phenyl]sulfonyl]glycine,
N-[[4-[[(4-Guanidinobenzoyloxy)phenyl]sulfonyl]glycine,
N-[[4-[[(4-Amidinobenzoyloxy)phenyl]sulfonyl]-L-phenyl-alanine,
N-[[4-(Benzoyloxy)phenyl]sulfonyl]-β-alanine,
N-[[4-(4-Amidinobenzoyloxy)phenyl]sulfonyl]-β-alanine,
N-[[4-(Phenoxycarbonyl)phenyl]sulfonyl]glycine,
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-L-phenylalanine,
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-L-aspartic acid,
N-[[3-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]glycine,

N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]glycine,
N-[(4-Methoxycarbonylphenyl)sulfonyl]glycine,
N-[(4-Carboxyphenyl)sulfonyl]glycine,
N-[[4-(4-Amidinophenoxycarbonyl)phenyl]sulfonyl]-β-alanine,
N-[(4-Benzoylmethylphenyl)sulfonyl]glycine, and
N-[4-[(4-Methoxybenzoyl)methyl]sulfonyl]glycine,

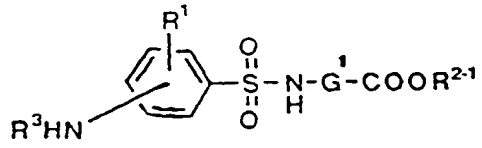
and esters and non-toxic salts thereof.

9. A compound of formula (Ib) according to any one of claims 4 to 8 or a non-toxic salt thereof for use in the prevention and/or treatment of a disease induced by overexpression or excess activity of a matrix metalloproteinase.

10. A compound of formula (Ib) according to any one of claims 4 to 8 or a non-toxic salt thereof for use in the prevention and/or treatment of a disease induced by overexpression or excess activity of a matrix metalloproteinase, which disease is a rheumatoid disease, arthrosteitis, unusual bone resorption, osteoporosis, periodontitis, interstitial nephritis, arteriosclerosis, pulmonary emphysema, cirrhosis, cornea injury, metastasis, invasion or growth of tumor cells, an autoimmune disease, a disease caused by vascular emigration or infiltration of leukocytes, or arterialization.

11. A process for the preparation of a compound of formula (Ib) according to any one of claims 4 to 8 or a non-toxic salt thereof, which process comprises:

(1) (a) reacting a compound of formula (IIb-a):

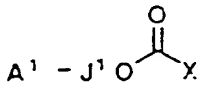


(IIb-a)

wherein R^{2-1} is C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl, $-OCOR^{16}$, in which R^{16} is as defined in claim 4, or $-CONR^{17}R^{18}$, in which R^{17} and R^{18} are as defined in claim 4, G^1 is as defined in claim 4 for G, with the proviso that R^6 and R^7 in G are not -COOH, amino, hydroxy or a group containing -COOH, amino or hydroxy, and the other symbols are as defined in claim 4;
with a compound of formula (IIIb-a):

$$A^1\text{-}J^1\text{-}COOH \qquad \text{(IIIb-a)}$$

wherein J^1 and A^1 are as defined in claim 4 for J and A, with the proviso that substituents of Ar in A^1 are not -COOH, amino, hydroxy, or a group containing -COOH, amino or hydroxy; if necessary, followed by deprotection; or
(b) reacting a compound of formula (IIb-a) with a compound of formula (IIIb-b):

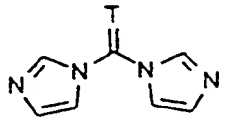


(IIIb-b)

wherein X is halogen and the other symbols are as hereinbefore defined; if necessary, followed by deprotection; or
(c) reacting a compound of formula (IIb-a) with a compound of formula (IIIb-c):

$$A^1\text{-}J^1\text{-}NHR^3 \qquad \text{(IIIb-c)}$$

wherein all the symbols are as hereinbefore defined:
and with a compound of formula (IVb-c):

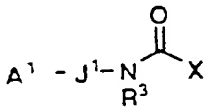


(IVb-c)

wherein T is oxygen or sulfur: if necessary, followed by deprotection;
or reacting a compound of formula (IIb-a) with a compound of formula (IIIb-c1):

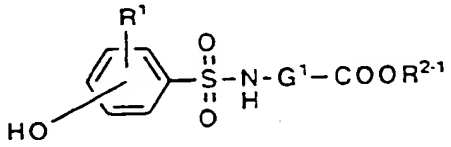
$$A^1\text{-}J^1\text{-}N{=}C{=}O \qquad \text{(IIIb-c1)}$$

wherein all the symbols are as hereinbefore defined; or with a compound of formula (IIIb-c2) :



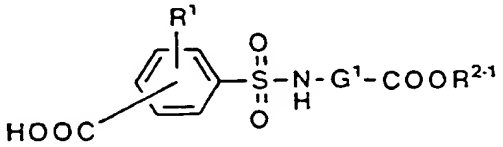
(IIIb-c2)

wherein all the symbols are as hereinbefore defined: if necessary, followed by deprotection; or
d) by reacting a compound of the formula (IIb-d):



(IIb-d)

wherein all the symbols are as hereinbefore defined;
with a compound of formula (IIIb-a); if necessary, followed by deprotection; or
(e) reacting a compound of formula (IIb-d) with a compound of formula (IIIb-b); if necessary, followed by deprotection: or
(f) reacting a compound of formula (IIb-f):



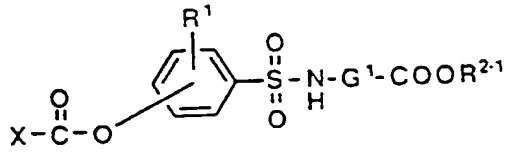
(IIb-f)

wherein all the symbols are as hereinbefore defined;
with a compound of formula (IIIb-c); if necessary, followed by deprotection; or
(g) reacting a compound of formula (IIb-f) with a compound of formula (IIIb-g):

$$A^1\text{-}J^1\text{-}OH \qquad \text{(IIIb-g)}$$

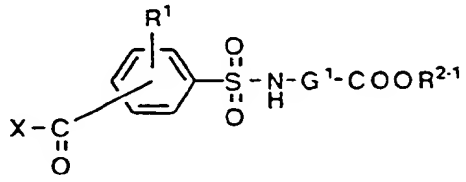
wherein all the symbols are as hereinbefore defined;

if necessary. followed by deprotection: or
(h) reacting a compound of formula (IIb-h):



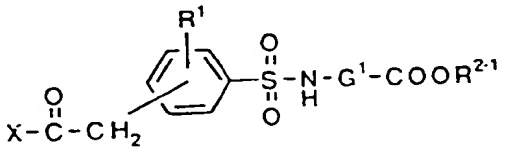
(IIb-h)

wherein all the symbols are as hereinbefore defined;
with a compound of formula (IIIb-c): if necessary, followed by deprotection; or
(j) reacting a compound of formula (IIb-j-1):



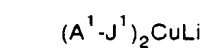
(IIb-j-1)

wherein all the symbols are as hereinbefore defined;
or a compound of formula (IIb-j-2):



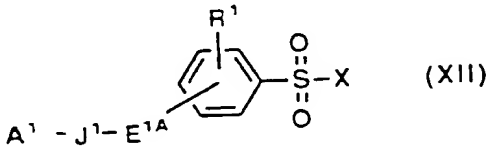
(IIb-j-2)

wherein all the symbols are as hereinbefore defined;
with a compound of formula (IIIb-j):



(IIIb-j)

wherein all the symbols are as hereinbefore defined;
if necessary, followed by deprotection; or
(j-1) reacting a compound of formula (XII):

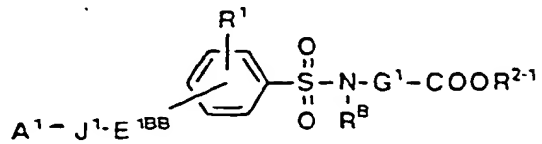


(XII)

wherein E^{1A} is -CO-NR^3-, -O-CO-NR^3-, -NR^3-CO-O-, -CO-O-, -CO-CH_2- or -O-CO-O-, and the other symbols are as hereinbefore defined;
with a compound of formula (XIII):

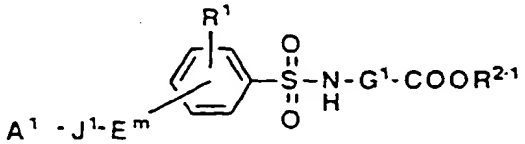
$$H_2N\text{-}G^1\text{-}COOR^{2\text{-}1} \qquad \text{(XIII)}$$

wherein all the symbols are as hereinbefore defined:
if necessary, followed by deprotection; or
(j-2) conversion of -NH- into -N($R^{3\text{-}1}$)-, wherein $R^{3\text{-}1}$ is C1-4 alkyl, phenyl or C1-4 alkyl substituted by phenyl; in a compound of formula (Ib-1-AB1):



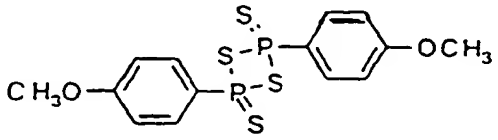
(Ib-1-AB1)

wherein E^{1BB} is -CO-NH-, -NH-CO-, -NH-CO-NH-, -O-CO-NH- or -NH-CO-O-, R^B is an amino protecting group and the other symbols are as hereinbefore defined;
followed by deprotection of the amino group protected by R^B; or
(k) reacting a compound of formula (Ib-m):



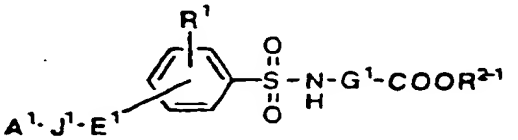
(Ib-m)

wherein E^m is -CO-NR^3-, -NR^3-CO-, -NR^3-CO-NR^3-, -O-CO-NR^3-, -NR^3-CO-O-, -CO-O-, -O-CO- or -O-CO-O- and the other symbols are as hereinbefore defined;
with Lawesson's reagent of formula (IIIb-k):



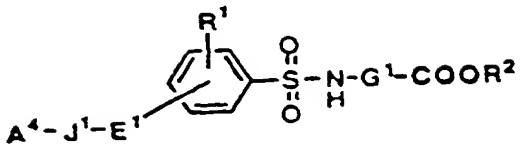
(IIIb-k)

if necessary, followed by deprotection ; or
(2) subjecting a compound of formula (Ib-1):



(Ib-1)

wherein $R^{2\text{-}1}$ is C1-8 alkyl, phenyl, or C1-4 alkyl substituted by phenyl, -$OCOR^{16}$, in which R^{16} is as hereinbefore defined, or -$CONR^{17}R^{18}$, in which R^{17} and R^{18} are as hereinbefore defined; G^1, E^1, J^1, and A^1 are as defined in claim 4 for G, E, J and A, with the proviso that when E^1 is -OCO- or -OCS- and J^1 is a bond, A^1 is not hydrogen; and with the proviso that substituents of Ar in A^1, and R^6 and R^7 in G^1 are not -COOH, amino, hydroxy, or a group containing -COOH, amino or hydroxy; and R^1 is as defined in claim 4; to deprotection; or subjecting a compound of formula (Ib-4):



(Ib-4)

wherein A^4 is as defined in claim 4 for Ar, with the proviso that A^4 is substituted by at least one nitro group, and the other symbols are as hereinbefore defined: to hydrogenolysis:
optionally followed by the conversion of the compound of formula (Ib) thus obtained into a non-toxic salt thereof.

12. A pharmaceutical composition which comprises a compound of formula (Ib) according to any one of claims 4 to 8 or a non-toxic salt thereof and a pharmaceutically acceptable carrier.